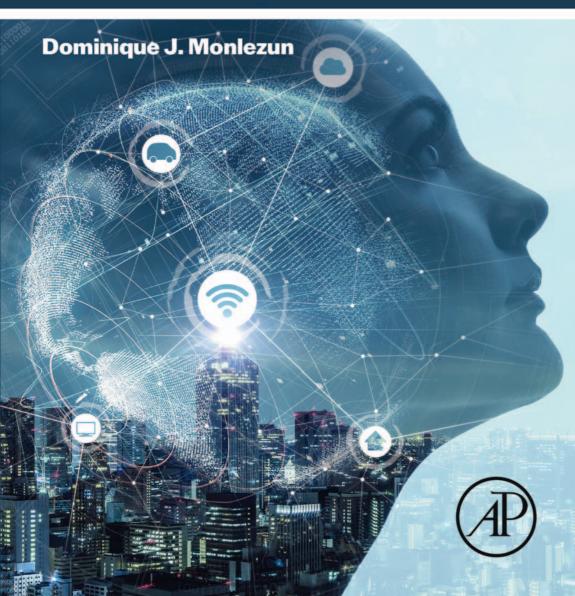
The Thinking Healthcare System

Artificial Intelligence and Human Equity



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Artificial Intelligence and Human Equity

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Dedication

To Mary, who started this whole thing.

To Susan, Lucy, André, and Jude—you are the best of me.

To my parents, siblings, and extended family, for showing me some things are worth fighting for.

To Dr. Colleen Gallagher,
Dr. Cezar Iliescu, Dr. Alberto Garcia,
Dr. Timothy Harlan, Dr. Richard Velkley,
Dr. Rebecca Mark, Dr. Shane Courtland,
and Dr. B.—your mentorship echoes in
every one of my pages.

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Chapter 1

Healthcare systems: challenges, crises, and cures

1.1 Background, purpose, and structure: why is this worth your time?

Hurricane Harvey slammed into the Texas coast in August 2017, hurling winds of over 130 mph, rain of over 60 inches, death to 107 people, and \$125 billion in damage (tied as the costliest tropical cyclone in United States [US] history) (NHC, 2018). But I still had to get to my patients at our hospital. But there was rapid flooding all around my home (with my wife and daughter evacuated the week prior to safety in the next state). The water had come up so quickly that it trapped many of us in our homes, making streets undriveable for cars. Spying a break in rain bands, I threw on my wet suit and boots, stuffed my little girl's baby photos beside my stethoscope against my chest, and began what became a 4-h trek wading in growing flood waters up to chest deep, passing military helicopters making search and rescues, camera crews trying to make sense of the chaos, and finally reached my Houston hospital in the world's largest medical center (whose size and technology could not make it immune to the historic storm laying siege to it). Once there, I stripped down to my scrubs and went to round on my patients as they needed me as their physician, as I needed them.

The memory since made me wonder—is this the story of modern health-care? The surging health toll and financial costs of diseases, poverty, pandemics, climate change, and wars appear to slam as determined and repetitive waves into our healthcare systems globally. Though there are flashes of coordinated progress and exciting artificial intelligence (AI) technological breakthroughs in our systems, it is questionable if we can point to any consistent, sustained, and substantive progress toward truly effective, efficient, and equitable healthcare for all patients. So in this book, can we journey together through the flood waters of the historical, global, and technological trends shaping healthcare, while identifying successful emerging solutions to them, to ultimately arrive at a more complete, concrete, and actionable blueprint of and roadmap to the future's optimized healthcare system? Can we analyze the challenges and crises defining modern healthcare currently, and

determining how its future evolutionary phase can respond successfully with the treatment and (even to some degree) cures for them?

But most relevant for you, why is this book worth your time? Because it is a series of first in content, methodology, and application. It serves as the first known book to provide substantive diagnosis of why healthcare systems globally are insufficient for humanity's needs, and the practical treatment for how to at least begin to sustainably, efficiently, and equitably reverse this trend (powered by effective AI and its related strategic ecosystem of collaborative competition) in our AI-driven digitalizing world. It therefore is the first comprehensive book detailing the historical, global, and technical trends shaping the evolution of the modern healthcare system into its final form—an AI-driven thinking healthcare system, structured and functioning as a global digital health ecosystem. Though AI is widely argued to be humanity's last great invention, as all subsequent ones will come through it, no single resource has yet explored and explained its associated revolutions producing the 'last healthcare system.' As the world's first triple doctorate trained physician-data scientist and ethicist, permit me to propose to you a shared theoretical journey through the above content, grounded in the day-to-day reality of what many books discuss but few if any live with an accuracy and precision enabling actionable improvements. The perspective of a physician (caring for patients at the bedside) who also is a data scientist (creating and deploying the algorithms meant to advance that care) is meant to facilitate the book being as academically rigorous as practically accessible to the broad audience required to transform (and even save) modern healthcare. Additionally, this book seeks to supersede other AI health books by providing a global approach that considers in depth not just the high-income countries and dominant power players in healthcare and AI, but also the low- and middle-income countries and emerging influential actors who traditionally have been excluded from equitable sustainable development and engagement. The multidisciplinary content, integration methodology, and practical perspective therefore seeks to maximize the unique value-add of this book, synthesizing the cutting-edge insights from a library of competing works while still advancing them into new waters to allow you to see further and act more confidently in the right direction. Regardless of your background, this work is meant to be your definitive, accessible, and internationally applicable resource for chartering an efficient and reliable course in the AI-digital transformation of the future's healthcare system (at the intersection of technology, organizational management, public policy, political economics, and multicultural ethics).

To achieve this function, the book's form is structured like the medical texts used to train physicians globally: we will seek to understand the trends, components, and relationships of the above which collectively generate healthcare systems (in their external and internal challenges and their emerging solutions) like the organ systems of the human body (in how they function internally and in relationship externally with other organs). This 'horizontal integration' or

breadth of knowledge will also be complemented by a 'vertical integration' of depth, synthesizing multiple disciplines. Consider how the treatment of a disease requires its accurate diagnosis and proportionality to the disease: to fix what went wrong we have to understand what part of the healthy functioning of the body became unwell and how to correct it. And understanding diseased or abnormal functioning of organ systems requires not only understanding the underlying biology, chemistry, and physics within each person, but also the politics, economics, and morality in which populations of persons exist. Accordingly, we will consider the historical, global, and technical advances in the AI-driven healthcare transformation of the 21st century in the dimensions of the 'organ systems' of healthcare systems: precision medicine (PrMed), public health (PubHealth), telehealth, patient safety, political economics, and ethics. To keep the book's scope sufficiently focused to allow actionable progress toward optimizing healthcare, the twin organizing principles of the book's above structure will be AI-driven efficiency and equitable gains of that efficiency across populations.

1.2 Rationale: avoiding the graft rejection and omitted variable traps

The rationale for the above content, methodology, and application is to avoid the twin traps which plague other AI health books: (a) graft rejection and (b) omitted variable:

- (a) In healthcare, 'graft rejection' is when the immune system of a transplant recipient attacks the transplanted tissue or organ (meaning often lifelong immunosuppression drugs are required to 'force' the patient's body to accept the graft, though at the risk of permanently lowered immune response to infections). Similarly, many expensive and embarrassing failures of businesses, governments, and healthcare systems throughout the last 3 decades integrating AI with healthcare have demonstrated that the medical community often sees AI as a 'graft' which does not naturally belong to the 'recipient' of healthcare systems and yet is still 'forced' upon it. Written from the integrated perspective of a physician who is also a data scientist, the book attempts to demonstrate in concrete use cases in each chapter how AI can be not only successfully joined with healthcare systems, but how it can come about through a 'natural,' embedded, transparent, and trustworthy codesign between clinicians and AI scientists and engineers.
- (b) In data science, 'omitted variable' is a common problem particularly in the dominant workhorse statistical technique of multivariable regression in which a relevant explanatory variable is not included as an independent or predictor variable in a regression which may subsequently fail to predict sufficiently and reliably the dependent or outcome variable (by biasing the

coefficient or measure of association of other predictors of the outcome). If I try to predict the odds of dying from lung cancer (outcome), then my results would be likely widely and rightfully criticized as unreliable and inaccurate if I only used such variables as age and income while omitting smoking history (as being older and wealthy enough to afford cigarettes is not nearly as important as actually smoking in terms of increasing the odds of developing and then dying of lung cancer). Similarly, many of the above expensive and embarrassing failures of AI and health integration over the years have omitted key predictors of integration success or failure. Written simultaneously from the dual perspective of a data scientist who is also a practicing physician, the book attempts to also demonstrate how technical solutions to clinical and organizational problems in healthcare can be tailored in ways that are unknown to the healthcare system affiliates who often struggle to articulate their needs to the AI community given their unfamiliarity with key aspects of AI.

This book respectfully proposes not only that there is fundamental compatibility between AI and healthcare systems, but also that AI is the natural next phase in the evolution of healthcare systems, and that in some notable ways, AI is most at home in healthcare of all societal sectors. Medicine is the most humane of the sciences, and most scientific of the humanities (Pellegrino, 2011). It is essentially a personal endeavor, occurring within the concrete context of a knowledgeable human provider encountering a vulnerable human patient, with the goal of health (considered as a good) of the person. It thus entails the personalization of the sciences (particularly biology, chemistry, physics, mathematics, and system engineering) to the unique needs of the person in front of the provider. AI, insofar as it is emerging potentially as our most powerful human technical invention (with the explicit purpose of increasing efficiency typically through optimized prediction), thus does not require it to be 'forced' into the healthcare encounter. The clinician simplifies and synthesizes her/his medical knowledge into her/his best educated prediction to what the most accurate and precise diagnosis is for the patient, and what therefore is most likely the best treatment for her/him. Good health AI is therefore what the good healthcare relationship already essentially is cognition and compassion translated into personal service to the human person.

Contemporary global crises including COVID-19 and climate change highlight some of humanity's greatest achievements—and failures—as well as those within healthcare. Those failures, ranging from tragic large-scale loss of life to worsening societal inequities, are only exacerbated by our own failures to adapt and redesign next generation value—based healthcare systems (VHSs) that are efficient, effective, and fair, and so better positioned to respond to the next wave of shared crises and challenges. This book therefore out of practical and ethical urgency *must* become the series of firsts described above to accelerate the solutions and even cures we are failing to deliver in healthcare at

sufficient consistency and scale. From the 1900s integrated healthcare system to the early 2000s VHS to the 2020s and beyond 'thinking' healthcare system, the emerging model of healthcare holds unprecedented (and concurrently under- and overhyped) promise for the global human community by harnessing AI, information technology, and globalized markets to predict, adapt to, and learn in real-time patient and population needs. This book is thus meant to unlock this potential for the next generation of patients, providers, payors, policymakers, politicians, and populations to ultimately bring us to the last or 'caring' healthcare system in which technology, economics, and justice are consistently leveraged to deliver on patient and population needs.

1.3 The book's defining value-add + audience

The unique features of this book include the following: its comprehensiveness (uniting the above topics for the first time in an accessible manner), technical mastery (understanding these topics and making them understandable for a broad audience), and societal urgency (giving a concrete blueprint and roadmap for how to respond to immediate and impending global crises and challenges to which we are still attempting to react to let alone understand and respond effectively, equitably, and proactively). No book has defined the last healthcare system, nor how to reach it, until now in this book. And no author has the integrated theoretical and real-world clinical, technical, and ethical background to bring those diverse perspectives into a single clear and compelling story that is robustly verifiable and globally actionable. The worldwide AI craze (from academics to governments to corporations to the public) and the increasingly influential role of healthcare systems in society particularly since the COVID-19 pandemic emergence makes the above topics essential for modernity. And this book finally points the world to where it can look to understand our modern health problems and how to fix them through systems, particularly from a global multicultural and interdisciplinary perspective unique to the healthcare system literature.

This book empowers diverse stakeholders to advance modern healthcare systems to their final optimized form by showing the big picture of how diverse technologies, health trends, and disciplines fit together through AI to produce it. The book allows clinicians, scientists, engineers, payors, politicians, policymakers, academics, students, and the general public to understand each other's perspectives and insights, and how to collaboratively build together the future's healthcare system—which is a bold vision but also one that can and must be practically realized. It syncs smoothly with the researcher and practitioner's entire workflow, from conceptualization of the ideal complex system to its design, production, continuous quality monitoring and improvement, and organic (but also supervised) self-adaptation. The book's content thus solves the big picture question of what is the optimal healthcare system, and the small picture questions of how to make it a reality.

The primary audience is therefore students, researchers, and practitioners. For students, the book is particularly meant for undergraduates and graduates (especially medical, public health, business, and policy) who lack such a central resource. For researchers, it is meant at the MBA, MPH, and PhD level (in public health, health services, health policy, and economic research) and MD and DO level (including clinician-researchers in the above areas). The book finally targets practitioners (particularly healthcare system executives both mid- and senior level, politicians with a particular health focus, policy-makers, think tanks, and technology-focused corporations). The secondary and still critical audience is the general public, interested in the big societal trends shaping modernity which play out in a large part in healthcare systems as one of our era's primary drivers, both economically and culturally (defining and reinforcing values and goods).

Aside from disciplines, the book is written for an international audience, with careful attention paid to societal, cultural, and demographics nuances and trends in mind. It is thus meant to not only be an invaluable resource for the most influential contemporary healthcare systems and related regulatory bodies both in health and AI (principally in North America and Western Europe), seeking to understand how they need to adapt to survive over the next few generations. But it also is meant to serve as a guide for emerging and increasingly competitive healthcare systems in Southeast Asia (including India and China) and Africa where capital and/or demographic surges are occurring and are expected to increasingly compete successfully with (and in some cases surpass) the West in the near to intermediate-term. Central to the book is thus a multicultural respect for diverse belief systems and backgrounds, and a clear technical grasp on the modern trends shaping the healthcare system of the future which are increasingly global in scope and operation.

For practitioners, the book is also meant to satisfy diverse training needs across diverse industries (including healthcare delivery, research, leadership, financing, and regulation, in addition to corporate firms in social media, technology services, data science, engineering, communications, and marketing) by providing a substantive foundation (understanding modernity through the lens of the future healthcare system), analytic methodology (integrating the latest research in real-time through AI to drive continuous redesign and quality improvement), multiculturalism and justice (achieving the above with personalized respect for diverse cultures and belief systems within globalized integrated systems extending beyond strict healthcare delivery), and leadership (translating the above research into scalable and practical decisions to accelerate the realization of the future healthcare system in the respective niches of those trainees).

For students, the comprehensive yet still focused scope of the book enables it to be a sufficiently flexible and substantive resource for a broad range of academic courses. A representative sample of the book's use is in the increasingly popular interdisciplinary courses across related departments including

undergraduate departments (notably biology in the premedical tracks, engineering, biomedical engineering, public health, business, leadership, sociology, economics, politics, and prelaw), medical school, public health departments, graduate school business, and graduate school policy departments (with the related courses on complex systems, healthcare system design, delivery, finance, leadership, AI, population health, and data science). Additionally, healthcare system courses are required in virtually all the major health-related graduate schools (including medical, public health, and health-specialized business and policy) with a total new annual enrollment in the United Nations medical and public health schools alone exceeding 40,000. Combined with the new enrolled students in premedical college tracks among which healthcare system courses are among the most popular and often required, this number approaches over half a million new students every 4 years.

In summary, most competing works describe current healthcare systems. A few offer vague or high-level predictions. This book uniquely describes the probable and optimal future healthcare system. It does so by offering the path and destination of future healthcare (by understanding concretely what it must be to respond to patient needs [value + fairness]) and the means to it [AI + equities]). So let us get right into it on this shared journey. We will begin with an overview of healthcare systems below, followed by the subsequent chapter introducing AI and its high-level emerging applications for healthcare, and then we will explore the 'organ systems' of healthcare systems introduced above before finishing with the final chapter on the synthesized concepts and use cases filling out the 'bones' of what the future's thinking healthcare system can look like and how it can function through emerging concrete cases.

1.4 Foundational definitions and concepts

Let us together take a temporary step back to consider a common general framework (conceptually and historically) to understanding healthcare systems so we can approach how they can be optimized for the future. The World Health Organization (WHO) formulated the most commonly accepted definition of a 'health system' with its 2000 version: "all the organizations, institutions, and resources that are devoted to producing health actions" (WHO, 2000, p. xi; Arteaga, 2014). It broadened this conception in 2007 to "all organizations, people and actions whose primary intent is to promote, restore, or maintain health" (WHO, 2007, p. 2). Though admirable in scope and intention, such conceptions remain notoriously challenging to operationalize. Thus, the Agency for Healthcare Research and Quality (AHRQ), as the primary federal agency within the US Department of Health and Human Services for optimizing US healthcare's quality and safety (Kronick, 2016), produced one of the most influential concrete and consensus-based definitions of a health system in its "2016 Compendium of U.S. Health Systems": an organization uniting at least one physician group and one hospital through joint

management or common ownership to deliverer comprehensive care spanning primary and specialty care (AHRQ, 2017).

Yet still the term 'health system' remains overly broad to practically conceptualize, measure, and optimize. To take the WHO and AHRQ definitions on face value is to see our entire world as a health system, since everything affects our health for good or bad, from our schools to grocery stores to community meeting centers to churches to clinics to hospitals to parks and so on. It seems we have to reduce 'health systems' thus to 'healthcare systems' to concretely and productively consider what makes for the 'good' healthcare system in a way that we can improve it when its deficits prevent it from achieving its end goal of delivering healthcare. (We will go more into this necessary and broader conception of what makes something good or bad, ethical or unethical, healthy and not healthy in the ethics chapter through a definition and defense of a globally convergent conception. But for the initial more technical and scientific chapters, we will focus on the above relevant aspects in the context of system). Across our diverse communities and cultures, we commonly say someone is a 'good' or 'bad' doctor insofar as she/ he approaches or distances from our common standard of what makes a doctor 'good' or 'bad.' And we commonly say something is healthy or not healthy insofar as it corresponds to our general conception of what good and bad functioning of an individual and society are (composed of individuals and their relationships connecting them together). Now it is (far) beyond the necessarily limited scope of this single book to show what is healthy or not healthy, or what is a good or bad health system (i.e., the totality of our individual and societal factors that collectively account for health or pathology as the good or deficit functioning of what it means to be an individual and society functioning well physiologically, emotionally, psychologically, communally, and so on). But we can to a degree describe what a good healthcare system is and can be for the future (and how AI can help us achieve it) by addressing the primary relevant factors dealing with how the goods and services provided within identifiable healthcare systems when done well can thus help deliver the ultimate object and objective of a good healthcare system-namely, good healthcare. This end or purpose is thus the ordering principle for the system's constitutive components (of payors, providers, and payors).

A healthcare system essentially delivers healthcare as goods and services according to its fundamental constitutive relationships of patients, providers, and payors. Persons become patients by seeking healthcare from system providers in the inpatient (hospital), outpatient (clinic), or community settings who are then reimbursed by payors (insurance companies, government funding agencies, cost-saving organizations, or self-funded patients). Yet there have been seismic technological, demographic, and societal trends that have increasingly shifted the historical trajectory of healthcare systems by changing the composition and relationship among patients, providers, and payors as the conception of healthcare has concurrently changed.

1.5 Historical development

Healthcare systems largely emerged as modern means of achieving the end of healthcare delivery as healthcare became more technical, effective, and complex, requiring increasingly complex supply chains, stakeholders, and parties to generate this supply for the simultaneous growing demand for it. Healthcare began potentially as early as Ancient Egypt around 1600 B.C., per the Edwin Smith Papyrus (named by Smith, its modern collector after its archeological discovery) as the first known surviving trauma surgery treatise copying a much older original text from around 27th century B.C. (Wilkins, 1965; Breasted, 1930). It is generally credited to Imhotep (Ancient Egyptian: *ii-m-htp*, "the one who comes in peace") as the first known 'physician' or practitioner of the medical sciences whose duty it was to restore the perceived disorder within the patient and thus the larger natural and supernatural order (Osler, 2004, p. 12). This tradition developed into some of the earliest instances of medical prescriptions in the Third Dynasty of the 22nd century B.C. Sumerian Empire of Ur in the modern-day Middle East (Biggs, 2005). Then by the 10th century B.C., Esagil-kin-apli (the ummânū or chief scholar for the Babylonian king, Adad-apla-iddina) produced one of the most comprehensive ancient medical texts up to that point named the Sakikkū (English: Diagnostic Handbook) (Heeβel, 2004, pp. 97–116). It formalized how healthcare was delivered by formulating the ancient Egyptian and Babylonian developments of the medical sciences, entailing a systematic approach to reasoning from empirical observations of observed signs and symptoms in patients to diagnoses, prognoses, and treatments using herbs, creams, bandages, and even eventually surgeries (Heeßel, 2004, p. 99).

As the medical sciences developed further, physicians provided healthcare goods and services to patients while training new physicians in some of the earliest known hospitals including in the ancient Greek asclepeions (Ancient Greek: Ἀσκληπιεῖον, "healing temples") by at least 500 B.C. (Askitopoulou et al., 2002), where Hippocrates generally recognized as the "Father of Medicine" trained at the asclepeion of Kos (Garrison, 1966, pp. 92-93). Similar centers developed in what is now modern-day India (Legge, 1965), Sri Lanka (Aluvihare, 1993), and Iran (Söylemez, 2005). Christianity adapted this ancient hospital template into its creation of the early forerunner model of the integrated modern healthcare system. Christian priests, monks, nuns, and laypersons, particularly after their expanded societal influence with their acceptance by the Roman Empire in the third century A.D., opened hospitals as charitable homes for the sick and poor, integrating them with the local Christian communities and ecclesiastical hierarchy who managed them to their development of an early societal welfare network of associated orphanages, schools, hospices, homeless shelters, and food distribution centers. State-funding linking governments and hospitals into healthcare systems were later seen by at least 1540 with England's King Henry VIII (Walter, 1878, pp. 359–363).

The explosion of the empirical sciences with the 16th century Scientific Revolution, societal emphasis on communal care with the 17th century Enlightenment, and manufacturing with the 18th century Industrial Revolution accelerated the development of the modern healthcare system. Following the devastation of World War II (WWII), the United Kingdom's (UK's) National Health Service (NHS) was created in 1948 as the world's first universal healthcare system, providing publicly funded primary and specialty healthcare to the UK population through NHS providers (Britnell, 2015, p. 3). This 20th century model of integrated healthcare systems (with state funding, regulation, and administration of healthcare services with varying degrees of private public collaboration) began to give way in the late 20th century and early 2000s to the VHS model given the exponential costs of surging technological advances, patient demands, and care delivery.

1.6 Value-based healthcare systems: health's future?

VHSs developed particularly in the US (the most technologically advanced and costly developed healthcare system) as an early 2000s alternative to the failed managed care organization (MCO) model of the 1990s. By that point, the US similar to many healthcare systems were compromised of a loose patchwork of private and public payor and provider networks, competing for a limited population of patients seeking the increasingly advanced and costly healthcare diagnostics, pharmaceutical (medicines), and procedural treatments (while patient populations particularly in developed nations became increasingly unhealthy from suboptimal health habits including tobacco use, excessive alcohol use, low physical activity, and poor nutrition [low in fruits and vegetables and high in sodium, fats, and sugar]) (Chemweno, 2021; CDC, 2022). Inflation for healthcare costs thus surged to the double digits even by the 1990s, prompting many private employers to transition their employees to MCOs attempting to control costs, while still delivering on patients' desired quality healthcare products and services through increased system efficiency and effectiveness (Shortell and Hull, 1996, pp. 101-148). The MCO tactics of limiting healthcare plan options, covered providers, and covered healthcare (by financially incentivizing providers to reduce offered healthcare products and services) ultimately undermined the MCO focus pressuring providers to compete on the basis of affordable quality healthcare (Robinson, 2001). The resultant backlash among consumers (as patients 'consuming' healthcare products and services according to the classical modern economics terminology) led to the general abandonment of MCOs by the early 2000s. Companies shifted to attracting employees with increased healthcare benefits (by access and range of products and services), which conflicted with foundational MCO tactics. This trend gained traction in parallel with providers' increasing successes pressuring MCOs to fund their enhanced volume-based competition among each other for increased patients through their own enhanced

healthcare access and range of products and services, regardless of the rising costs or questionable quality of that healthcare (Lesser et al., 2003).

Amid this historical headwinds, accountable care organizations (ACOs) in the 2000s became the strategic descendant of MCOs by seeking to outlive their predecessors through by sharing the same strategy (optimizing quality and cost) but through enhanced tactical (and semantic) focus on care coordination, continuous quality improvement, and integrated data analytics (bridging financial claims [requests for healthcare reimbursement to a payor] and patient health records [detailing of healthcare delivered by providers]) (Tu et al., 2015). In this model, payors seek to financially incentivize providers networked within ACOs (which can consist of providers groups, individual healthcare systems, and networked healthcare systems) to demonstrate clinically effective and cost-efficient healthcare management of a population rather than simply the volume of healthcare delivered to individuals. Payors shift the financial risk of managing patients and patient populations to providers within an ACO, which in turn is financially rewarded by greater profit sharing if it delivers greater savings to payors in the course of delivering quality healthcare to its patients. By 2021, US ACOs grew to number 477 organizations caring for 10.7 million patients and saving \$2.4 billion for the Centers for Medicare and Medicaid Services (CMS) (the largest US healthcare payor and the primary government national health insurance program) (King, 2021).

Thus enters VHS. The push for 1990s MCOs (publicly perceived to focus more on restricting patient choice) largely was rebranded and retooled in the push for the 2000s ACOs, which in turn gave way to the 2010s (early adopters and larger scale up in the 2020s) VHS model under the banner of 'value' (marketed and reportedly managed to finally optimize net benefit for patients and their payors). Michael Porter and Elizabeth Teisberg's seminal 2006 formulation of value-based healthcare laid the groundwork for the subsequent steady surge in healthcare system transformation into VHSs including globally (Porter and Teisberg, 2006). Their central argument is that modern healthcare costs are exploding out of control (with the quality of that care remaining inconsistent and inadequate at best) because competition in free market capitalist economies (which largely dominate the contemporary world for the last century and for the foreseeable future) is misplaced. Healthcare competition historically has been focused among payors and providers (offering more and more services, produces, and access) when it should be occurring at the level of concrete health improvements per unit purchased. Healthcare systems should thus compete among each other to demonstrate to patients and their payors why they deliver superior healthcare improvements through superior diagnoses, treatments, prevention, and costs relative to their peers. Better healthcare for better cost = value-based healthcare. Over the subsequent 2 decades, value-based healthcare has grown into the dominant model for optimal healthcare system design, in parallel with increased global pressure for healthcare payment reform from the traditional fee-for-service (incentivizing

providers to provide more but not necessarily better healthcare products and services with an emphasis on acute treatment at the individual level) to population-based global payments (incentivizing providers to provide more clinically effective and financially efficient care across the entire care continuum with an emphasis on prevention and chronic condition management at the population level) (Ginsburg and Patel, 2017).

Value within this model is defined as the improvement in a patient's health outcomes (achieved by empirically measured quality plus perceived level of service divided by the cost of that healthcare) (Teisberg, 2020). Value-based healthcare has since become the dominant model of contemporary healthcare and thus of the VHSs delivering that valuable healthcare. Getting better patient outcomes for less cost at least in theory should satisfy all involved stakeholders-patients, providers, and payors (or at minimum make them the least unhappy relative to alternative outdated models of healthcare and healthcare systems). The essential operational features of VHS include patient segmentation (identifying subgroups of patients sharing common healthcare needs), interdisciplinary healthcare design (with diverse stakeholders within the provider community identifying the healthcare products, services, and related delivery mechanisms as the required means to achieve the ends of meeting the above needs), and quality improvement (through a continuous feedback loop in which health outcomes and costs generated by the above inform redesign or refinement of the system and its strategy-informed operations). The VHS model is thus data and analytic-intensive as better outcomes are aggressively sought through better data-driven insights and resultant decisions. The technological trends (increasingly advanced but costly diagnostics and treatments), demographic trends (aging populations with increasingly complex healthcare needs), and societal trends (populations demanding more of the above healthcare) increasingly solidify the outsized influence the model of VHS has on contemporary (and foreseeable) healthcare delivery. The trends thus underline the significant financial incentive for modern healthcare systems to integrate AI to manage the exponentially increasing data speed, volume, and complexity (which the next chapter will consider) to get to increasingly accurate, precise, and real-time system design and operations.

1.7 Politics, economics, and regulation

Healthcare systems are intrinsically embedded in, shaped by, and influence their sociocultural context. Healthcare is a good which has simultaneously an individual dimension (as it is used by an individual patient) and public dimension (as the type of healthcare a patient seeks is influenced by societal values influencing individual choice, while the provision of that healthcare requires a complex relationship of diverse actors and societal forces outside of the just the individual receiving the healthcare). Politics, economics, and regulation arise from this dual dimension of healthcare at the system level and manifest both unique regional and common global aspects.

Internationally, the growing dominant push for value-based healthcare increasingly drives healthcare systems in developed and developing nations to incorporate the growing global foci on (a) digital transformation; (b) public health integration with healthcare systems; (c) mental wellbeing; (d) environmental, social, and governance; (e) medical science technological development; and (f) health equity (Deloitte, 2022). Economic pressure on modern healthcare systems for cost containment and quality optimization has led to their gradual transition into and incorporating ACOs, and now increasingly into value-focused healthcare systems built upon the above pillars (which the COVID-19 pandemic following 2019 only accelerated). The universal economic pressures translate into global political pressure at the state, regional, and community levels for healthcare systems to respond to their trends. Intrinsic financial and extrinsic political forces conceptualized as the contemporary value-based health ecosystem globally and locally thus are pushing healthcare systems to: (a) connect inpatient, outpatient, and home care through digital cloud services (with data collection, storage, analytics, and decisions) and telehealth; (b) open healthcare systems to prepare for and respond to wider health influences (housing, education, public safety, etc.) and shocks (pandemics, wars, etc.); (c) recognizing and addressing the mental toll of healthcare deficits and of mental health deficits on healthcare; (d) broaden system focus on its ecological impact on patient needs through enhanced system energy efficiency, resilience against environmental disasters, and responsiveness to patient needs worsened by ecological challenges; (e) balancing investments in medical science research and development with the larger system responsibilities for cost containment and health equity reduction; (f) and leverage the above to identify and reduce health disparities concurrent with accurate and respectful embrace of a more holistic and comprehensive vision of health (including its clinical, mental, emotional, physical, social, and spiritual dimensions which diverse patient communities may value and be deprived of differentially). Regulations operationalize generally accepted standards of the above in terms of explicit definitions of those standards, relevant providers required to adhere to those standards, criteria for those providers to demonstrate compliance, and punishments and disincentives for providers who excessively deviate from those standards. Typically, these regulations are defined and enforced by centrally recognized bodies with law-enforcement capacity (such as with the US CMS and professional credentialing associations for physicians) which trickle down to the healthcare system level that usually add their own system-specific regulations for their providers (such as with competency and performance requirements for providers to keep hospital privileges to care for patients within the system).

Regionally, there are a number of unique political economic features that differentially impact their related healthcare systems (ten Have, 2015, pp. 147–150). Contemporary modernity's dominant political economic ideology of neoliberalism (in contrast to socialism, communism, conservatism, and fascism) through its free-market capitalist economic structure and liberal democratic political structure accelerated post-WWII globalization, with its most recent manifestations in the post-Cold War Internet of Things (IoT)based global digital ecosystem. The explosion in sophisticated medical technologies initially dominated healthcare systems' focus and management as patients were offered increasingly advanced diagnostics and treatments. But as we have already noted above, their resultant cost explosion drove cost containment and then value-focus, leading to developed nations' healthcare systems increasingly championing value-based healthcare. And while there is notable trickle down of their technologies, strategies, and operations in developing nations (including through the globalized reach of many of these healthcare systems and relates supply chains spanning developing and developed nations), this technological and value orientation in modern healthcare systems deepens the divisions between developed and developing healthcare systems. Developed systems in their management, regulation, and related ethics initially centered (in the early maturation of this 1970s political economic phase of system development) on the impact of the medical sciences and technologies on system potential. Building in the 1990s and 2000s and only speeding up since, these developed systems increasingly focus on the impact of societal inequities driving health inequities particularly among lower income and racial minority communities serviced by healthcare systems. Such inequities grew as liberal political economic trends internationally among developed nations led to more privatization of healthcare systems and related welfare safety networks of programs, leading to decreased healthcare access, affordability, and inequities among such communities (particularly those vulnerable to the negative health impacts of poverty and external shocks like pandemics, wars, and climate change). Such health inequities within developed healthcare systems are distinct from the health inequities within developing healthcare systems. The later have decreased access to the latest medical sciences advances and technologies yet with often greater system efficiency (which affords the 'luxury' of focusing on greater population-wide value rather than simply a basic set of healthcare products and services for the most vulnerable communities falling through the 'cracks' of the developed systems preferentially benefiting higher income communities).

A particularly stark recent example of these intersystem health inequities framing much of the interactions between developed and developing health-care systems is the COVID-19 vaccine nationalism. The developed nations spanning the US and European healthcare systems designed, tested, and manufactured the most scientifically advanced vaccines to date for any disease through the mRNA-based COVID-19 vaccines in record time, and yet with-held the needed distribution of them to developing nations during the critical initial phases of the pandemic, despite the projected global cost of this nationalism reaching \$9.2 trillion total (Çakmaklı et al., 2021). Rich nations received 84% of the first year of all COVID-19 vaccines, while 1.1% of low-

income nations received them (leaving the rest typically in manufacturing and stockpiling outside the reach of the latter). Further, developed nations achieve a \$4.80 return on investment (ROI) for every \$1 they spend providing developing nations with vaccines, while rich nations in doing so reduce their likelihood of being hit by more dangerous viral variants (which otherwise are more likely to mutate through unvaccinated lower income communities before traveling to richer communities and nations). Still, the WHO throughout 2021 and 2022 faced stiff resistance as it pleaded with rich nations to permit the needed vaccine supplies and means of production to reach the rest of the world (Hafner, 2020; UN, 2021; World Bank, 2021). The Director of the Africa Centres for Disease Control and Prevention (CDC), Dr. John Nkengasong, argued this vaccine inequity in developed versus developing healthcare systems (as one of the most urgent and stark contemporary health inequities) demonstrates the "collapse of global cooperation and solidarity" (Myers, 2022). Such health inequities exacerbated by the underlying global political economic context are increasingly shaping the current and projected future relationship of healthcare systems globally. Failing to address such inequities places growing political economic pressure on the world's diverse healthcare systems to collaboratively identify and improve clinically effective, cost effective and societally equitable value-based healthcare (particularly in the face of such global challenges as pandemics that respects no divide between rich and poor, developed and developing, high- vs. low-performing healthcare system). Such pressure underlines the international consensus about the conceptual shift of value-based healthcare to include the world's developing and developed systems, increasingly seen as a single global (even superficial) network of providers who have shared responsibilities to collaboratively serve the shard end or goal of value-based care to the entire global human community of patients. Failing to do so is not simply bad healthcare, it can be bad political economics as the consequences affect everyone.

1.8 Present problems: poor quality, safety, prevention, and cost

We have so far taken a big picture look at healthcare systems including in their foundational concepts, terminology, history, and sociocultural-based political economic context. Now we can start diving into more of the concrete specifics about emerging trends that are shaping their present, trajectory, and future.

1.8.1 Present problems: poor quality

The WHO defines quality healthcare as achieving "desired health outcomes" by being effective (providing evidence-based healthcare appropriate to patient needs to optimize desired outcomes), safe (avoiding harm to patients in the above process), and person-centered (respecting patient needs, values, and preferences as far as effectiveness and safety appropriately and feasibly permit) (WHO, 2020). The means of achieving the end/goal/objective of quality is by healthcare delivery being timely (proportional to patient needs), equitable (without quality variations according to nonmedical traits such as gender, ethnicity, and socioeconomics), integrated (linking prevention, acute, postacute, and chronic care throughout patients' lives), and efficient (avoiding waste). When healthcare deviates from the scientifically determined, broadly ethical, and expert consensus-based definition of standards of evidence-based healthcare, quality is compromised.

What quality is can be largely clear but not how to actually reach it, as modern healthcare systems have struggled delivering quality care since it first was systematically defined and measured (despite its delivery being the primary objective of healthcare systems), as this struggle is generally recognized not just by providers (executives and clinicians) but also the public (patients, payors, and policy-makers) (Berwick, 2020; OECD, 2019; Bates and Singh, 2018; Schneider et al., 2017; Black, 2013; Rozenblum et al., 2011; McGlynn et al., 2003; Brennan et al., 1991). Empirically, patients may receive only half of the evidence-based standard of healthcare for acute and chronic health conditions on average, with as little as 10% for such conditions as chronic alcohol dependence (McGlynn et al., 2003). It would be interesting to see if the world would tolerate any of the other leading economic sectors like energy and automobiles having approximately a coin toss likelihood in delivering what their consumers demand. (How often would we attempt to tank up our vehicles at a gas station if the pump only turned on randomly half the time, or electric vehicles randomly charged or did not charge when you plug them in?) And yet widespread underperformance in healthcare quality continues to plague healthcare systems globally, which can often be obscured under claims it is too complex or challenging to do otherwise.

Exactly where does healthcare quality currently stand? The first joint global report from the WHO, OECD, and World Bank describes the contemporary global scale, depth, and consequences of modern systems' quality deficits, pervasive at all income levels for systems and nations (WHO et al., 2018). Healthcare systems across high-, middle-, and low-income nations commonly struggle with incorrect diagnoses, medication errors, unnecessary and inappropriate treatment, unsafe clinical practices and facilities, and insufficiently trained healthcare providers. Despite quantitative differences of these quality challenges across systems and nations, there is a qualitative commonality of these threats being prominently present. For instance, hospitalized patients in low- and middle-income nations have a 10% likelihood of developing an inpatient healthcare-associated infection (HAI) which is higher than in highincome nations (but only by 3%). So approximately 1 of every 10 patients entering a hospital to receive care will be harmed on average by also receiving an infection (despite it usually being effectively and cheaply prevented through such simple interventions as consistent hand-washing by providers). Even in

high-income nations, nearly 15% of hospital costs are due to medical error and HAIs. The report further highlights the rate of inaccurate diagnoses may be as high as 75% (particularly in low- and middle-income African nations). Effective healthcare for children (one of the most clinically and cost-efficient sectors of healthcare systems with among the highest societal ROI) may be as low as 21% for sick child care and 28% for antenatal or before birth care, particularly in lower income African and Caribbean nations. Piecemeal progress in quality (including decreased cardiovascular disease [CVD] and cancer morality) is eclipsed by growing health, economic, and social costs from poor quality's effects including chronic impairment and disability with subsequent decreased productivity—topping trillions of dollars a year worldwide. Decreased healthcare quality reduces human economic quality which undercuts poorer nations and systems' capacity for growth and improvement, leading poor patient care to perpetuate poor population health and thus exacerbate societal poverty and inequities.

Are modern healthcare systems getting better responding to this foundational challenge of quality underperformance? No (vs. not by much) it seems. Most of healthcare systems' multidecade efforts in quality improvement focus on middle- and high-income communities, which constitute over 70% of the global population and witnessed doubling of costs from 2000 to 2016 alone, without any significant commensurate change in quality for the majority of our planet's patients (Barber et al., 2019). Further, small pilot tests for quality improvement generally fail to successfully scale up to the population level (such as with surgical checklists seeking to standardize quality coming up short at reducing procedural complications and mortality) (UN, 2021). Healthcare systems struggle to even measure quality accurately and precisely in ways relevant to patient populations (Black, 2013). Such measurement is further undermined by the general omission of patients in the process of identifying patient healthcare expectations (Rozenblum et al., 2011). Even nations with universal health care fail to consistently achieve equitable access (OECD, 2019). A 2019 WHO and OECD report supports how the complexity of care delivery in healthcare systems, patients' divergent acuity of illness, and lack of price transparency complicate effective political and economic pressure from populations to successfully push for sufficient and equitable quality optimization (Barber et al., 2019). The historic WHO-OECD-World Bank joint report highlights how quality can be improved through such straightforward strategies as government funding and regulatory focus on universal healthcare with clear quality standards, healthcare system improvement in patient experience and competent care augmented with transparent quality analytics, and patient populations' engagement in healthcare system design and reform. But executing these strategies with effective tactics has proven elusive thus far (WHO et al., 2018).

1.8.2 Present problems: poor safety

A landmark British Medical Journal 2016 study suggests medical error may be so prevalent that it ranks as the third leading cause of death (Makary and Daniel, 2016). The authors of this study advised it be interpreted cautiously given the widespread disagreement among healthcare researchers, administrators, policymakers, and patients about what are sufficient safety metrics (that are valid, accurate, precise, and relevant) (Jha and Pronovost, 2016). Such disagreement extends to the classification of what constitutes preventable errors that fall short of those safety metrics. Even experienced clinical reviewers on this topic may reach only moderate interrater agreement about the occurrence of an adverse event, its contribution to mortality, and if it could have been preventable (Smits et al., 2009). Yet accurately defining preventable errors are critical to the central objective of healthcare systems as noted above—to deliver quality healthcare to patients (which first and foremost should be safe by delivering more desired good than undesired bad outcomes). And thus the growing body of related research has been seeking to establish consensus-based metrics and standards to guide effective policy and administration for health systems.

Toward that goal, one of the pioneering studies in this field found that up to 4% of hospitalized patients may experience adverse events, with 78% of fatal errors being preventable (Leape et al., 1993). Subsequent studies confirmed this rate may be consistently nearly 50% (de Vries et al., 2008). Such adverse events may cause over 2.6 million deaths in low- and middle-income nations (NAS, 2018). Up to 40% of patients internationally may be harmed with outpatient healthcare, including 80% of such cases being preventable (Slawomirski et al., 2018). The principal cause of these preventable errors is rarely negligence but rather insufficient system capacities for safety. Blaming providers for 'doing the wrong thing' is not enough. The rapidly expanding complexity of healthcare delivery increases the likelihood of the most common errors (including in prevention, medication, diagnosis, and surgeries, with the most preventable errors being the last two). When too many smaller errors coincide to produce a major safety failure, adverse (even fatal) events can occur. James Reason's Swiss Cheese Model has since become the primary methodological framework for analyzing and improving such medical error and safety measures by understanding healthcare delivery like a block of Swiss cheese (Reason, 2000; Perneger, 2005). Each safety precaution is like a slice of cheese that no matter how rigorous, still has holes. If too many holes line up, an adverse event can occur by making its way through the entire block to impact the patient on the other side.

Substantive global efforts continue among healthcare systems seeking to optimize patient safety, particularly after the US Institute of Medicine's 1999 To Err is Human report first elevated this issue to a high-profile, institutionalized focus (Bates and Singh, 2018). Such efforts typically demonstrate proof of efficacy in small test cases (particularly in reducing diagnostic errors, medication errors, and HAIs), but they often fail to scale to the needed system and state levels (usually amid barriers to consistent and sustainable implementation limiting sufficient response to the complexity of the interrelated safety challenges). Consider a patient in her/his biological context as a complex organism of interdependent biological processes and organ functioning. If the heart suffers a sufficiently massive myocardial infarction or 'heart attack,' it can drag all the other organs down with it—just fixing the heart and then moving on to the next organ then the next may be too simplistic, slow, and ineffective to save the dying patient (the provider instead has to simultaneously and aggressively treat the multiorgan failure that can rapidly kill the patient). Similarly, a modern healthcare system requires a multipoint and parallel arm approach to prevent and fix the interdependent errors arising from the complex interdependencies of the system components (which organically produce the net 'vector' or end-result of healthcare delivery for patients). So the scale, speed, and complexity of healthcare delivery correlate with the scale, speed, and complexity of its related preventable harmful errors—challenges that the safety research community increasingly are turning to health information technology and AI to address (as ways to quickly analyze the rapidly expanding scale, speed, and complexity of health data to design, test, and improve more effective safety improvements efforts which can then quickly scale, optimize, automate, and institutionalize them in systems). The WHO's 2021 master strategic action plan for accelerating global patient safety detailed how systems' growing electronic health record (EHR) utilization allows unprecedented digitalization of patients and populations' health and related financial data in a way that increasingly allows AI to quickly screen, detect, and prevent harm (WHO, 2021, pp. 55-61). Importantly, such AI-based risk stratification and reduction methods can be developed at higher income healthcare systems and states and then be tailored and scaled at lower income systems and states with lower EHR utilization to more equitably share the benefit of this emerging paradigm of AI-driven safety improvements (more details on this in the next chapter).

1.8.3 Present problems: poor prevention

Sickness and disability are like biological wars—they can be urgent, dangerous, and costly. Prevention is far preferred over treatment for maximum clinical effectiveness and financial efficiency for patient and population health. Historically, healthcare systems have been paid for the more healthcare services and products they deliver to patients—not for achieving better health at lower costs for patients and populations with those services and products. Prevention has thus been increasingly prioritized as healthcare systems evolved from patchworks of providers in the early 1900s to Health Maintenance Organization (HMO) in the 1990s to ACOs in the 2000s and VHSs in

the 2020s beginning to finally scale value-based healthcare at the population level. Growing evidence demonstrates the superior quality and cost of such prevention-focused value care. Such a care model empirically appears to outperform alternative models at slowing healthcare cost inflation and increasing quality (Song et al., 2019; McWilliams et al., 2014, 2015, 2018; Nyweide et al., 2015). Payors give a lump sum to providers in this model to care for a patient population. Providers are further rewarded with financial incentives from payors through retaining shared savings if they spend less than the allotted budget, in addition to quality bonuses for improving value care (to thus disincentive withholding appropriate medical care). Providers on the flip side must bear the cost if they spend more than what is allotted for the population, and if they fail to effectively prevent acute complications of insufficiently managed chronic health conditions. CVD (the leading medical cause of death globally) costs the US alone \$363 billion in healthcare services, medicines, and mortality-related lost productivity (Virani et al., 2021). Yet up to 28% of acute complications from CVD may be prevented through increased consumption of a Mediterranean diet (Ahmad et al., 2018). Cutting CVD costs in one nation by over \$100 billion annually just by modifying what patients consume (as they must already eat something) is difficult to ignore.

How do healthcare systems do with prevention? Poorly, on average. Less than 10% of health expenditures targets prevention (in the world's most advanced and expensive national network of healthcare systems), though the majority of health outcomes are due to modifiable health behaviors (particularly diet, physical activity, and tobacco consumption) (McGovern, 2014). A high-profile systematic evaluation of 195 nations in Lancet strengthened prior evidence demonstrating that poor diet is the world's top modifiable risk factor for mortality, small dietary changes have the maximum diet benefit (through increased fruit and whole grain and decreased sodium consumption), and such improvements may internationally prevent 1 of every 5 deaths (GBD Diet Collaborators, 2019). This study additionally demonstrated that deaths worldwide may be reduced by 2% for each optimized consumption of primary components of the 9-point Mediterranean diet (including whole grains, fruit, vegetables, nuts, and omega-3 fatty acids). Systematic review evidence supports how adopting a Mediterranean diet does not necessarily increase weekly foods costs (and appears may actually reduce them on average) but does significantly reduce healthcare-related costs through reduced burden of disease (Saulle et al., 2013).

The largest study of provider nutrition education and first study on culinary medicine demonstrated providers and clinical trainees through a hands-on cooking and nutrition education curriculum can effectively be instructed in how to provide Mediterranean diet counseling to patients, and that patients' Mediterranean diet consumption improves when those providers then teach patients through those nutrition-based cooking courses (Monlezun et al., 2022). This curriculum in its first 5 years was able to cost-effectively provide

over 24,680 h of hands-on cooking and nutrition education to over 4051 medical students, physicians, and patients at 45 medical schools, hospitals and colleges (nearly 1 in every 4 US medical schools). A randomized controlled trial demonstrated that this curriculum compared to the standard of medical care and education reduces families' food costs while tripling their odds of consuming a Mediterranean diet (particularly for lower-income families) (Razavi et al., 2021). A separate randomized controlled trial with the above control supports that the curriculum produces superior reduction in patients' diastolic blood pressure and cholesterol, two key predictors of adverse CVD outcomes (Monlezun et al., 2015). This scalable capacity-building intervention for healthcare prevention targeted physicians and medical trainees because of the leading role these providers fill in healthcare system delivery, the sustained patient diet modification based on physician counseling, providers' inadequate standard training in counseling patients on nutrition, and the improvement from this curriculum in current and future providers' competencies providing patients nutrition counseling while improving their own diets (Monlezun et al., 2018). Like much of the quality improvement attempts in healthcare systems globally, effective prevention-focused interventions that can be scaled and institutionalized increasingly appear to be the most successful and sustainable interventions (Dixon-Woods and Martin, 2016). Though the above suggests a promising paradigm for building prevention capacity for modern healthcare systems, there is limited expansion thus far to middle- and low-income nations and systems (and minimal direct financial incentives for providers to continue dietary counseling in practice).

1.8.4 Present problems: poor cost

We have thus far considered the central problems of poor quality, safety, and prevention posing the greatest present challenges for healthcare systems. Now we will consider how they culminate in poor cost control (perpetuating and exacerbating the above problems). Globally across nations, systems, and belief systems, health is generally understood as the most foundational societal good and necessary economic pillar. No life, then no economics nor society. Empirically, healthcare is one of the most influential economic sectors, the world's largest economic sector behind only energy and automobiles, includes 2 of the top 10 largest companies internationally by annual revenue (the US CVS Health and UnitedHealth totaling nearly \$0.5 trillion alone), accounts for nearly 1 of every 5 dollars of the gross domestic product (GDP) of the US (the world's largest economy), and employs 1 of every 10 workers (Fortune, 2021; Nunn et al., 2020). And if an explosion can accelerate, that is what is happening to modern healthcare costs. Global consensus across payors, providers, and patients (in addition to corporations, policymakers, and politicians) is that healthcare inequities, aging populations, increasing chronic disease prevalence, healthcare waste, and costlier innovations in new medications, procedures, and technologies are only worsening this unsustainable surge (Kimpen, 2019). Consider the US where these trends are among the most stark internationally. Healthcare costs per capita quadrupled from 1980 to 2018, approximately half of national healthcare costs come from only 5% of patients, costs for privately insured patients vary up to 3 times higher for certain regions compared to others for comparable healthcare independent of patient age and disease burden, and post-ACA (Affordable Care Act) market consolidation is increasingly geographically concentrating costlier specialists and hospitals (Nunn et al., 2020; Bernard 2012; Cooper et al., 2019; Capps et al., 2018; Gaynor, 2020; Heisler et al., 2018).

The US spends more of its GDP on healthcare than any other nation, and as the top economy globally, it would be expected to have among the best performing healthcare systems—yet it ranks as the worst performing system among high-income countries (Schneider et al., 2021). Across 71 performance measures using WHO and OECD data, the US comes in last in healthcare access, administrative efficiency, health equity, and health care outcomes (while spending more than any other nation to 'achieve' these poor outcomes). The top performing nations (Norway, Netherlands, and Australia) in contrast excel through four common features: (a) primary care prioritizing prevention over acute care; (b) universal health coverage expanding equitable access; (c) shunting administrative investments to value-based care delivery; (d) expanded societal safety net emphasizing children and working-age adults (which reduces the chronic disease burden and its related frequency and severity of acute complications and societal impact). This comprehensive approach conceptualizing healthcare broadly as a societal good and operationalizing it locally appears resilient to what appears to be the leading cause of death globally (poverty, with its associated manifestations in poor education and social support), which is not simply a significant medical problem narrowly defined but also a profound societal challenge (Galea et al., 2011).

This poor system and cost performance is notable despite 11 years of significant institutional and financial investment following the US President Obama's ACA (Obamacare) passed as the most significant healthcare expansion and regulation revamp since Medicare's 1965 creation (Blumenthal et al., 2015; Cohen et al., 2015). Obama's political party, the Democrats, has since acknowledged the best contemporary opportunity to revive American healthcare reform efforts (namely the first 2 years in office of Obama's Vice President at the time and since the 46th US President, Joe Biden, and his fellow Democrats controlling the legislative and executive branches of government) has largely passed with no clear path forward amid intense competition among conflicting political and economic interest groups (Kane, 2022; Smith, 2022). The previous reform attempt of Medicare Advantage plans meant to salvage Medicare (as the first major American medical program to expand and improve US healthcare) through HMO-style administration by private payors 'privatizing' government health insurance—has repeatedly

demonstrated cost increases without clear and sustained quality enhancement (Kronick, 2021; Herd, 2021; Jacobs and Kronick, 2018; Kronick and Welch, 2014). The US appears to not only spend the most per capita in the world on ineffective, unsafe, and inequitable care, but also the most trying to (at least thus far) inefficiently fix it. It seems new solutions are needed.

1.9 Emerging solutions: digital, personalized, globalized, fair

Now that we have considered the primary present challenges to healthcare systems, let us consider the emerging potential solutions which may shape the future of healthcare that is digital, personalized, globalized, and fair. The common engine in these four vehicles of change is AI-driven digitalization, but to get to the engine, we need to first sketch what, how, and why it is increasingly used for this change.

1.9.1 Emerging solutions: digital

Modern healthcare's digital transformation into the future's healthcare system is the primary catalyst and probable determinant of what it will look like and how it will operate (Appleby et al., 2021). And this digital transformation can be traced back to the arguable standard of modern healthcare which developed with it. In the terrible, silent aftermath of an 1883 tornado which nearly destroyed an unknown rural American town, a Catholic nun approached the town doctor with the plea to open a hospital they would fund if he and his sons would care for its sick (Blistein and Burns, 2018). In the ensuing years, the father and sons recruited more physicians to respond to the growing needs of their growing number of patients, resulting in an ever expanding list of pioneering innovations which helped shaped modern healthcare—the integrated multispecialty practice model, the personalized medical record, sterile surgical tools and operating rooms, the first graduate medical education program, the first nonprofit medical practice networked with medical education and research (Clapesattle, 1941; Bruce, 2015; Grayson, 2016; Becker's staff, 2014). That hand-shake partnership of Dr. William Mayo and Mother Alfred Moes has since grown into Mayo Clinic, the present top ranked modern hospital and healthcare system (remaining a leading contender for that rank for the last 3 decades) and best performing academic medical center by valuebased healthcare, generating \$15.6 billion annually in revenue (Harder, 2021; Luckstein, 2021; Ernst and Young, 2018). In 2013, Mayo partnered with Optum (a data and care division of UnitedHealth, America's largest insurance company or private payor) to form OptumLabs with a 150 million patient deidentified clinical and claims (financial) dataset, specializing in AIaugmented real-time insights into care improvement as part of a continuous feedback loop of continuous quality improvement (Wallace et al., 2014).

Since Mayo's early development of the medical record to its current global version as the EHR, 80% of its contained patient data is physician notes, leaving the vast majority of healthcare shrouded from traditional analytics (Rosenbilt, 2018). OptumLabs through Mayo's support has become a world leader in this digital health transformation as it "turn[s] artificial intelligence into health care intelligence," accelerating value-based care through optimized personalized, effective, safe, and affordable diagnosis and treatment augmentation by learning from millions of population-level records. From the 1883 tornado wreckage-turned-hospital to the 2022 digital revolution, modern healthcare has sought to come full circle back to the patient, listening to the patient's needs and seeking to respond individually at the point of care and systematically by redesigning the healthcare system around the patient to more effectively respond to the next such patient. It is not a perfect but a promising (and working) solution.

How concretely is digitalization emerging as a healthcare solution for the future's healthcare system? (a) Personalization, (b) transparency, (c) standardization, (d) convenience, and (e) value. The IoT-augmented global digital ecosystem allows unprecedented integration of digital mobile devices, EHRs, and other diverse data sources to accelerate (a) AI-based personalization of standards of care at the individual patient level including through more robust prevention, rapid and accurate diagnosis, and effective and equitable treatment the healthcare system digitally integrating the patient's home, food sources, schools, businesses, community organizations, clinics, and hospitals (Chén and Roberts, 2021; Zimlichman et al., 2021). (b) Healthcare systems are globally and broadly critiqued for the lack of transparency of price, quality, outcomes, and equity (Zimlichman and Levin-Scherz, 2013; Kimpen, 2019; Zimlichman et al., 2021). This subsequently limits informed patient/consumer choice and thus effective public pressure challenging systems to compete on the basis of value created for consumers; digitalization is steadily reversing this trend by quantifying and reporting metrics relevant to consumers, payors, and reporting bodies increasingly 'ranking' systems for improved consumer choice.

Personalization and transparency improving value healthcare requires (c) standardization of value metrics and their consistent utilization, which digitalization force multiplies by driving data capture, algorithmic analysis, and common denominator reporting uniting diverse stakeholders in healthcare systems (from clinicians to administrators to vendors) with a common language and means to improve the common outcome of value for the patient. This grounds healthcare systems on the trajectory toward value-based healthcare, including with the standardized "Quadruple Aim" of "value measure" formalized by the Philips Future Health Index: improved patient outcomes and experience through improved provider satisfaction and cost (Philips, 2021; Porter et al., 2016; Kimpen, 2019). The Fourth Industrial Revolution of the digital ecosystem integrating disruptive technologies (like AI-based IoT, cloud computing, robots, 3D printing, quantum computing, and

nanotechnology) with the biological and physical worlds is finally breaking into healthcare with its emphasis on equity, following COVID-19 accelerating the market trend of patients as consumers seeking convenience in healthcare, prompting systems to accelerate such digital-based services like telemedicine and mobile app-based EHR access (Deloitte, 2022; Ndung'u and Signé, 2020). Digitalization therefore unites the emerging trends of personalization, transparency, standardization, and convenience to produce the ultimate end and objective of value-based healthcare (concurrently becoming the organizing principle of healthcare systems); systems increasingly are pressured to deliver and demonstrate healthcare that operationalizes allocative (equitable), technical (effective), personal (satisfying), and societal (communal) value by operationalizing the above strategic and technical trends (Rosalia et al., 2021).

1.9.2 Emerging solutions: personalized

Healthcare systems are pivoting to this future digital-based age of healthcare by increasingly quantifying, centralizing, and seamlessly analyzing the diverse aspects of healthcare and patients to allow more precise application of standards of care (derived from population-level studies and standards) to the individual to make healthcare personalized and so effective for patient needs and responsive to demands. The predominant contemporary practice in healthcare systems is for providers to personalize the standards of care (largely defined by association guidelines and the latest generally accepted research) using their "clinical judgment" for the patient. Yet the above quality section detailed how ineffective, inefficient, and inconsistent this provider-dependent personalization is. Digitalization as introduced above increasingly is utilized to bridge this gap by informing and augmenting provider-based delivery of healthcare concurrently with automating and institutionalizing this delivery at the system level. Provider-driven personalization is limited by the slow, location-dependent data (which mostly consists of in-person and in-clinic or inpatient vitals, exams, laboratory values, imaging, and biopsies that are labor intensive to measure, digitize, and upload to the EHR). Increasingly, patients' mobile or wearable digital devices like the Apple Watch (measuring heart rate and rhythm) and continuous glucose monitors (as part of close hybrid loop systems for patients with type 1 diabetes measuring real-time glucose linked to their insulin pumps and smart phone apps, which subsequently adjusts insulin rate up or down) allow unprecedented real-time, longitudinal, uninterrupted immediate data collection, storage, and analysis (Perez et al., 2019; Brown et al., 2019). Such digital-based self-monitoring and patient-level application of population datasets not only enhance the digital health ecosystem (linking mobile data with the above traditional health data in the EHR) for systems and providers to have more of a comprehensive understanding of the individual patient, it already has immediate clinical benefit. Perez et al., for example, demonstrated that it boosted detection of previously undiagnosed atrial

fibrillation (a known mortality risk factor) by 34%, and Brown et al. showed it increased time in target glucose range (a known predictor of morbidity-free survival) by 12%.

This person-specific, real-time, large-scale, and longitudinal selfmonitoring thus enhances digital-augmented personalized healthcare by empowering patients to better understand their health and healthcare needs, providers to better diagnose and treat based on population-level standards of care, and for systems to better tailor services at the community level for similar patients (Li et al., 2017; Chén et al., 2020; Murray et al., 2016; Widmer et al., 2015; Peng et al., 2021). Effective and equitable personalized healthcare can further be tailored with digital devices and population dataset application integrated with traditional EHR data by tracking patient-specific treatment responses and side effects compared to population averages for similar patients, yet significant optimization to the above workflow is still required (Agarwal et al., 2021; Xu et al., 2019; Chawla and Davis, 2013).

1.9.3 Emerging solutions: globalized

The above quality section already introduced how the world's top performing healthcare systems take a globalized approach to patient care, caring for the patient as a person who is a member of the local and international community of humanity (linked by common needs and means of delivering on those). The World Economic Forum provides an emblematic example of one of the leading global models of such healthcare: Future of Health and Healthcare (FHH) (WEC, 2022). FHH seeks to accelerate the transition from the current clinically and cost inefficient hospital-based healthcare delivery to digital ecosystem-based healthcare integrating personalized prevention and care delivery (across the care continuum) by integrating homes, clinics, hospitals, and the rest of the built environment. This transition is operationalized by harnessing the Fourth Industrial Revolution (that increasingly is accelerating globalization of states, economic sectors, and individuals) and emerging private-public partnerships (which quickly identify, test, and scale best-inclass health innovations).

The COVID-19 pandemic has only catalyzed this transition further by demonstrating the failure of (and needed improvements in) collective global action on preventing, containing, and mitigating the pandemic specifically and emerging global healthcare challenges more generally (Barlow et al., 2021). COVID-19 powerfully demonstrated we are citizens of a globalized world, and thus so are our healthcare systems inescapably global at least in part in their influences, threats, and opportunities. Most systems even in higher income nations struggled in the early days of the pandemic to slow the spread and respond to strained global supply chains to source and deliver providers' personal protective equipment along with patients' treatments and vaccines (Alam et al., 2021). International consensus is that COVID-19 revealed the globalization

lessons for future healthcare systems developed by state-specific "whole-ofgovernment and whole-of-society approaches," emphasizing structural solutions (particularly to socioeconomic inequities), minimization of fragmentation (of diverse societal, government, and system components), public health system capacity building (in integrated healthcare systems), evidence-based and agile public health emergency governance (data-driven, clear, consistent, pragmatic, effective, and equitable), and ready national strategies (Assefa et al., 2022). Such globalization-driven emerging solutions for next generation healthcare systems extends beyond such challenges to urgent, persistent, and preexisting challenges that are global in scope (commonly experienced universally) and context (requiring collective and coordinated action among states, societies, and systems): societal inequities, climate change, pandemics, wars, etc. (Lavizzo-Mourey et al., 2021; Atwoli et al., 2021).

1.9.4 Emerging solutions: fair

The above sections have introduced how the Fourth Industrial Revolution is fundamentally altering our globalizing society not just economy (by orientating the integration of digital technologies and physical assets to equitable value within the new model of capitalism model of stakeholder capitalism, as corporations and governments collaborate for the shared social responsibility to persons, populations, and the planet in response to the growing universal public vision of our common humanity, home, and responsibility to each other) (Deloitte, 2020). Accordingly, the emerging model of the future healthcare system is being framed, driven, and informed by this revolution, including its emphasis on societal equity so the benefits of digital, personalized, and globalized value-based healthcare benefit persons proportional to their needs—to ensure healthcare systems are ultimately fair not just effective. Central to this fairness is payment reform, featuring a growing number and approach to such efforts, including value-focused ACOs, payment method, and pricing systems. Value-focused ACOs compared to non-ACOs have demonstrated lower costs for rural and underserved patients (Trombley et al., 2019), as have bundled payments moving away from the traditional fee-for-service model (incentivizing volume irrespective of quality or appropriateness at the patient-level) toward global payments (incentivizing value respective of affordable quality and equity across a population) (Barnett et al., 2019). Pricing overhaul is increasingly focused on improving healthcare system's free market-based competition and thus performance on the basis of value for patients and populations (including on fairness, rather than simply volume prejudiced to higher income individuals) by: data infrastructure investment, empowered price regulatory systems (independent and impartial overseeing healthcare systems), affordable sequential implementation (at a pace and scale affordable for systems' population of price, supply, and regulatory reform), efficient price setting (reducing waste and fraud through more transparent value-focused performance), appropriate national participation in price setting (with unilateral price setting by the centrally recognized regulatory system through collective negotiations and nationally implemented by political bodies accountable to democratic majorities, instead of price setting between buyers and seller's individual negotiations which can create regional monopolies irrespective of delivered value), and responsive real-time revision to system design and operations (allowing rapid and flexible policy testing, implementation, scale up, and redesign) (Barber et al., 2019; Berwick, 2020).

1.10 AI: from survival to sustainable healthcare systems

To respond to the historical and current healthcare system challenges of poor quality, safety, prevention, and cost, emerging solutions that are digital, personalized, globalized, and fair increasingly are framing the projected future healthcare system model to move systems from simply surviving to being sustainable (and societally responsible). Even high-income communities and nations are increasingly unable to afford today's exploding healthcare costs that generally deliver insufficient value for inflationary prices. Yet decades of attempted policy-focused healthcare system reform have mixed results at best. Interestingly, individual emerging outliers of high-performing VHS like those of Norway, Netherlands, and Australia in addition to the US Mayo Clinic indicate not only that healthcare can be effective, safe, affordable, and fair, but that the replicable solutions to get closer to it increasingly feature the AIdriven Fourth Industrial Revolution and its integrated digital ecosystem. Value healthcare systems appear to be a promising sketch of the future healthcare system, but how it can be operationalized and scaled sustainably is not yet clear. The AI-accelerated transformation from today's value healthcare systems (which are still provider-driven, hospital-centered, volume-orientated systems) to the future thinking healthcare system (that is person-driven, digital ecosystem-centered, value-orientated) thus appears to warrant testing if it is a viable shared path forward for us all and our healthcare systems (which the next chapter will consider).

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Chapter 2

AI + healthcare systems: efficiency and equity

2.1 Objectives and scope

As the last chapter sought to provide a concise overview of healthcare systems (with their past drivers, present challenges, and future trajectories), this chapter attempts to introduce the increasingly fundamental role artificial intelligence (AI) is playing in redefining, reframing, and revolutionizing the healthcare systems of the future by moving from an abstract conceptual to a concrete operational overview. In doing so, we will generally define AI, its current healthcare system applications, the justification for those applications, and its growing influences, implications, and trajectories. This chapter's sections will thus focus on defining AI then healthcare AI, before transitioning into the latter's data infrastructure and healthcare system integration, research and development (R&D), governance, workflow, system design and operation, and key power player. These seminal concepts and terminology will allow in subsequent chapters to zoom into the primary focus areas of present and future healthcare AI: its technical domains of precision and public (population) health linked by the delivery mechanisms of telehealth and remote engagement, as well as those domains' societal contexts of the digital health ecosystem, patient safety (and security), politics, economics, ethics, and globalized healthcare systems. This conceptual development is meant to ultimately bring us to the point where we can flesh out the expected healthcare system of the future: the thinking healthcare system. It should be noted that this task (and the persons, patients, and populations it is meant to serve) exceeds what can and should be definitively contained in a single book. To therefore limit the scope of our above objectives to a manageable but hopefully still informative degree, we will focus technically on what, how, and why AI is shaping the future of healthcare systems and societally how should it be doing so to optimize healthcare equities. An accurate technical account is required to advance healthcare at an operational level (allowing actionable knowledge of AI-driven healthcare system design and improvement). And a respectful, robust, interdisciplinary, and multicultural account is required to show how AI can defensibly (ethically, culturally, and legally) accomplish the above by

focusing on the ultimate aim toward fair and just care (that can effectively limit the book's scope and enhance its value for diverse audiences, particularly in our globalized world being remade by the Fourth Industrial Revolution focused on technological and equitable progress across systems, cultures, societies, and states).

We will thus introduce with increasing detail from this chapter onward how globally our world is moving from AI to AI in healthcare systems to AI healthcare systems. And so let us consider a common major objection at this point that otherwise prevents us from moving further: can we accurately, precisely, and definitively detail the future healthcare system? No. Can physicians accurately, precisely, and definitively detail the future of an individual patient? No. Does that stop the patient from seeking from the physician as accurate, precise, and informative a prediction for her/his future? No. It is exactly the future's uncertainty and present need to still make reasonable decisions that highlight the value for both healthcare systems and patients to have the most robust and reliable predictions as possible. As AI is increasingly doing for systems and providers do for patients, this book will proceed with caution and transparency to build the strongest predictions possible (to hopefully help guide the most reasonable decisions possible to optimize the likelihood of the most desired future). We will take our inspiration and course from the biology underlying healthcare—once we know how the human body and mind work, we can understand the diagnosis for when it goes wrong and to some degree the treatment to fix (or manage) it. Accordingly, the end or objective of healthcare systems as already discussed is to optimize health using the finite means of systematic delivery of healthcare through a network of aligned intellectual and material capital. If we know the inputs (patients), means (healthcare delivery), and intended outputs (health), we can to some limited degree (albeit that is still accurate, precise, and informative even if not definitively comprehensive) know the diagnosis and treatment for the system to become the optimal model for the future. By understanding where systems came from and where they are going (like understanding the sickness that is pulling a person from a prior state of health to a worse state of health without sufficient intervention), we can make the best educated guess possible where to intervene. The difficulty and complexity of the above task only reinforces rather than negates the urgency and possibility of such tasks being accomplished (and such a book focused on such a task) to understand healthcare systems currently, what their emerging model can and likely will be, and how to optimize the best versions of that model. Competence not certainty is a necessary prerequisite for me as a physician serving my patients who come for the best chance of healing; similarly, this book considers that competence accurately, precisely, and informatively defining and analyzing health systems' past and present allows us to provide a substantive and productive projection of their likely and desired future. Additionally, there is limited need to simply consider what healthcare systems are like now (they are more or less evident in

front of our eyes). We need to know where they are going tomorrow (and how to direct them to the commonly desired destination). And to keep the above tasks manageable in this limited text (and still hopefully helpful and actionable for you, the diverse audience to use to inform your important work within the unfolding of the future's healthcare systems) to reach this comprehensive map, our left foot will be AI (as the most transformative force in healthcare) and right foot will be human equity (as the major focus of the AI-driven Fourth Industrial Revolution largely determining healthcare's future trajectory) upon this shared journey (with such large claims as above which will be shortly better defined and hopefully sufficiently defended). Ultimately, to heal patients in the future, we are seeking if and how future healthcare systems need AIaccelerated organizational healing themselves to fulfill their mission (namely, the health of human civilization, and thus the possibility to sustain that shared future).

2.2 Al overview

AI is a broad field and term that describes the study and application of intelligent agents that receive environmental inputs and perform actions typically to optimize the likelihood of achieving a desired objective (Russell and Norvig, 2020, p. vii). Conceptually, AI is more machine-centric rather than human-centric intelligence—humans create machines that can autonomously "think" to augment human intelligence and actions. Practically, AI are machines (hardware like robots and software like algorithms, i.e., stepwise rules to perform a task) capable of varying degrees of perception, logic, and learning (Intel, 2018). Popularly, the most prevalent current AI is machine learning (ML), in which algorithms typically analyze large amounts of data to find patterns and associations among different factors that allow them to make predictions (on outcomes) and performance improvements (in those predictions as more data are digested). The most prevalent emerging AI is deep learning (DL), which generally is an artificial neural network (ANN) algorithm that requires little to no human design for it to make predictions, and even modifications to its design, by identifying the optimal approach to performing such tasks. An algorithm is a mathematical and computer science term describing a finite (or limited number) sequence of defined instructions to perform a computation, usually to solve a particular class of problems (Merriam-Webster, 2022). ANNs are computing systems modeled on the biological neural networks in animal brains (Winston, 1992). In an artificial network, units or nodes of artificial neurons (like the human brain's nerve cell) connect through "edges" (like the brain's synapses connecting different neurons) to transmit a signal or number(s) (like the brain's electrical conduction). A neuron receives the signal as an input and produces an output typically as a nonlinear function of the sum of inputs. Neurons and edges have weights corresponding to the strength or weakness of a signal that changes as learning

progresses. These neurons are often layered as signals travel from input to output layers. Such DL and the more basic ML are computing (compared to more material or robotic) AI, respectively, divided into supervised (with more human design and modification) and unsupervised (with less human design and modification) learning. Technically, AI can be divided into its primary function of translating inputs (or percepts) to actions: including DL, decision-theoretic, real-time, and reactive agents (Russell and Norvig, 2020, pp. vii—viii). Academically, AI is where math meets engineering, computer science, statistics, ethics, and law. Historically, AI has principally thus far been narrow AI (i.e., ML that is context-specific, focused on particular applications, and principally human-centric and driven), which increasingly is giving way to artificial general intelligence (AGI) (i.e., DL that is context-independent, open to diverse applications, and principally machine-centric and driven), which in certain domains is increasingly approaching or approximating the intellectual tasks accomplished by human agents (Kahn, 2021).

Societally, AI is rapidly altering the global human community by not only allowing unprecedented efficiency gains in our technology (increasingly framing and driving our overlying educational, scientific, cultural, economic, and political systems) but also presenting new existential challenges (including what truly separates man from machine, and whether AI can surpass humanlevel intelligence) (Barrat, 2013). Anthropologically, AI may be the most disruptive and revolutionary human technology given how fundamentally it is already redefining national security, governance, healthcare, finance, criminal justice, infrastructure, and communication, and how much potential left that it is expected to increasingly operationalize (West and Allen, 2018; Sallomi, 2015). A simple but influential current argument practically explaining this rapid and revolutionary grip AI is exerting on the larger modern world is that it makes prediction cheaper (Agrawal et al., 2018). Though the breadth and depth of AI's technical application and mechanism of its transformative force on modernity's various sectors and aspects are complex, the overarching economic framework explaining its impact is straightforward. Our personal, academic, business, societal, and political lives are constrained by uncertainty. Better prediction (of desired outcome) enables better decisions, outcomes (over time and on average), and strategies (defining and refining classes of decisions individually and structural approaches to problems collectively). Such enhanced prediction is particularly driven by AI's ML effectively integrating statistical methodologies and applications. As AI improves our ability to understand increasingly rapid, varied, and complex data, we can arrive at better predictions that unleash increased (and even explosive and unprecedented) productivity and efficiency. Yet such AI-driven progress can often be nonlinear, unpredictable, and opaque. Certain breakthroughs in certain sectors and situations may unpredictably be reached faster than others. This progress is often concentrated among a small number of AI actors (who have the economic and political capacities to afford the often-high costs of developing

and deploying the most technologically powerful AI). And it may produce often far-reaching unexpected societal effects generated through unclear mathematical mechanisms central to the AI (whose reduced transparency can further undermine societal skepticism of AI's impact as it is often unclear, i.e., how AI algorithms generated different predictions which then may guide political and business decisions). Consider how the US pharmaceutical company, Moderna, powerfully leveraged proprietary AI approaches to create, test, obtain approval, manufacture, and distribute one of the first and most effective COVID-19 vaccines (which are all thus exciting and impressive technical successes). Yet they primarily benefited the United States and richer developed nations during the most critical phase of the pandemic (Ransbotham, 2021; Hafner, 2020; UN, 2021; World Bank, 2021). AI not only can make the rich and powerful more rich and powerful, but they can do so at a rate that increases the distance between them and poorer, weaker actors (whether they be individuals, businesses, or governments). The subsequent sections and chapters will explore in the context of healthcare sectors this promising but still uneven AI rollout.

2.3 Healthcare Al overview

Despite the speed, scale, depth, and potential of the AI revolution in our modern world, there has been relatively little substantive adoption in healthcare thus far, despite the expected significant role it will increasingly play in the coming years—leading to the common expectation that healthcare is the last modern frontier for AI (Arndt, 2018). Nearly all of healthcare essentially is a function of prediction. Providers must apply biology and standards of care probabilistically to individual patients by assigning to them their most likely accurate and precise diagnoses and corresponding effective treatments. And the delivery of such healthcare occurs largely in healthcare systems according to administrators' probabilistic management of resources, that is, projecting how many emergency department (ED) providers are needed to handle the day's influx of emergency cases, which primary and specialized services a growing community will require over the next decade, and which innovative technologies and pharmaceuticals should be developed and acquired (like new telemedicine services and medications). If healthcare systems' primary objective is moving from current uncertainty about patient health needs to future outcomes delivering value responsive to those needs, and AI may serve as one of the most effective technological means to this destination (with greater speed, efficiency, and precision), it seems at least plausible that AI will play an increasingly fundamental role in healthcare systems' future.

From an overview standpoint, the three major domains of AI applications in healthcare (or healthcare AI) are patient-, clinician-, and management-oriented AI (Deloitte, 2019). The primary objectives in those domains respectively include increasing patients' streamlined engagement with and access to their personalized healthcare, providers' productivity of high-value care, and management's effective resource allocation and cultivation including of the workforce and emerging pharmaceutical products and care services.

The three major phases of healthcare AI development include testing, scaling, and revolutionizing (Deloitte, 2019). The principal activities in these phases respectively are identifying successful cases of largely ML-driven optimization of current healthcare and healthcare delivery practices, scaling those applications throughout systems, and ultimately integrating and institutionalizing those applications within existing system structures and workflows. That final revolutionary phase ultimately seeks (and is cautiously expected) to reach AGI-based real-time continual system redesign and optimization at the patient-, provider-, and system-wide levels allowing unpredictable and unprecedented leaps in productivity and value (and at least initial jumps in inequity).

The major tools of the current testing and emerging scaling phase of healthcare AI include ML and natural language processing (NLP), the latter which has recently begun effectively utilizing DL to process, organize, categorize, extract, analyze, and report on human-generated language texts. This allows AI algorithms to "understand" human language texts like an electronic health record (EHR), but at a scale and speed typically exceeding human capacity such as by analyzing millions of patient records simultaneously (Turchin and Builes, 2021; Deloitte, 2019). The primary desired (and practically possible) outcomes for patients through healthcare AI in the first two phases include optimized healthcare effectiveness, equity, access, choice (of products and services), convenience, speed and convenience (of integrated and streamlined care), and payment ease and affordability. The primary desired outcomes for healthcare system providers and managers include optimized patient well-being and satisfaction, workforce well-being and pay, system costs, wait times, error rates, adverse event rate, and financial sustainability relative to the larger healthcare competitive ecosystem (of similar providers and systems).

The major healthcare barriers to AI adoption include limitations in (a) data access, (b) algorithms, (c) incentives, (d) complementary innovations, and (e) regulations:

(a) Healthcare AI performance is currently significantly hampered by the scarcity of large, high-quality datasets (since such performance is largely dependent upon ML, the most effective and prevalent healthcare AI tool currently, which still requires such data), most healthcare data locked in EHRs (which are largely localized to healthcare systems with little compatibility and regulatory mechanisms allowing sharing, centralization, and standardization into integrated datasets), and insufficient provider buy-in for such process improvements (given the significant time such improvements require, pulling providers away from direct healthcare

- delivery amid limited apparent value added in the short term to justify this utilization of providers) (Reisman, 2017; Topol, 2019).
- (b) Algorithmic bias, as a "black box" AI phenomenon, also challenges wider healthcare AI adoption. Usually, the more advanced and effective algorithms entail less transparency in how the outcomes are generated. This undermines their interpretability and trustworthiness for skeptical audiences and a clear path forward to reducing their latent biases and undesired outcomes—especially considering the lack of generally accepted standards for effective and ethical algorithm design and performance to sufficiently reduce such bias satisfactorily for such audiences (Bembeneck et al., 2021; Stern and Price, 2020; Crawford et al., 2019).
- (c) There additionally appear to be conflicting incentives for various stakeholders in healthcare AI adoption, as the data scientists who typically develop AI algorithms and the system executives who direct and approve them may often seek productivity improvements (replacing to some extent providers), which conflicts with providers seeking to remain integrally connected with the personal delivery of healthcare to patients (who thus resist "being replaced by computers" especially when there is a lack of demonstrated evidence that such replacement is consistently safe or benefits patients) (Garnett, 2020; Budd, 2019).
- (d) Insufficient complementary innovations also slow healthcare AI adoption, similar to how the widespread adoption of EHRs and the internet required much larger system and society-wide innovations (i.e., integrated software systems, organization-wide vertical integration, streamlined workflow processes across diverse professions, performance pay, contractual alignment of supply chain stakeholders, and institutional buy-in) (Dranove et al., 2014; Forman and Gron, 2011; Breshnahan and Greenstein, 1996). The technical development and deployment of algorithms require an ecosystem of innovation in which there are widespread support and parallel (and often structural) advances such as those in
 - i. medical education (increasing provider knowledge, design and application involvement, and acceptance of healthcare AI);
- ii. performance (integrating standardized and centralized data infrastructures linking mobile, clinic, and hospital data);
- iii. payment (incentivizing providers and systems to successfully deploy AI to achieve healthcare value over traditional volume);
- iv. financing (supporting particularly lower income and rural healthcare system utilization of the often cost-prohibitive initial AI investments); and
- v. compatibility (streamlining different data infrastructures from different systems "communicating" with other systems and nonhealthcare data sources like social media, mobile devices, community organizations, businesses, and government sources in a publicly transparent and accepted manner).

- (e) Excessively outdated, voluminous, irrelevant, conflicting, and stringent regulations additionally limit healthcare AI adoption (often without clear and commensurate benefit for the communities meant to be protected by such regulation however well meaning), particularly in the following arenas:
 - **i.** privacy (as there is generally significant more public restriction of data sharing in healthcare than other societal and economic sectors) (Miller and Tucker, 2011);
- ii. medical technology (given the notoriously protracted time, intense scrutiny, and substantive investment to bring a new medical drug, device, and technology from design to approval [with an average cost to bring a new drug from design to testing to approval to market consumption being \$2.6 billion over 10 years, after surviving an 88% likelihood of failure] [PhRMA, 2015, p. 1]);
- iii. liability (as healthcare regulation is typically much more robust than other sectors due to appropriate concern for the greater personal stakes in adverse events and data breach, which can thus significantly challenge provider acceptance of such emerging AI capacities until they are more "proven") (Galasso and Luo, 2019, pp. 493–506); and
- iv. technology (given how AI can be and typically is significantly more rapid, unpredictable, and complex than most regulated sectors or technologies, as it is even conceptually challenging to consider how would a DL algorithm be regulated if it by design can to a degree "rewrite itself" [unlike a new medication's chemical formula] in ways that may not have been originally envisioned by its human programmers or prevented from producing longer term and more wide ranging societal effects than initially expected, especially given how such risks are more difficult to sufficiently convey to a nontechnical regulatory body).

2.4 Digital transformation of healthcare: healthcare Al's data infrastructure and system integration

2.4.1 Structure of the modern healthcare system

Now that we have considered an overview of AI and specifically healthcare AI according to their major concepts and trends, let us move progressively to healthcare AI's concrete and on-the-ground operational overview, beginning with its data infrastructure and integration with healthcare system operations. This is meant to provide a concise and practical map to healthcare's digital transformation. To go back to the medical analogy of the graft and host, we will consider broadly here how AI and healthcare systems can be technically compatible according to their similar technical structures, and how this compatibility enables their productive integration especially in terms of input, processing, storage, analytics, and decision-making.

A dominant conceptual model of the modern healthcare system can be adapted from Ferlie and Shortell's four nested levels that describe the system as the network of entities and their relationship accounting for the healthcare delivery: the individual person as a patient (first level), the provider teams (second level with the physicians, nurses, and other allied health professionals at the point of direct care, in addition to the pharmaceutical and medical technology, device, and supply organizations indirectly supporting the needed goods and services for the point of care), the organization (third level, with the aligned hospitals, clinics, nursing homes, home health and hospice agencies, and so on), and the sociocultural conditioned political and economic ecosystem (fourth level, including the payment, financial, and regulatory parties in addition to the larger societal ecosystem including the person's digital global community, local community partners and organizations, and home) (Institute of Medicine, 2005; Ferlie an Shortell, 2001). Given the historical development of healthcare systems described in the last chapter, the 20th century exerted significant pressure on their precursor components to aggregate and unify in modern healthcare systems that increasingly took shape in the latter half of that period as a "cottage industry." Productivity units like provider teams, clinics, departments, and hospitals operated in various degrees independently of each other with differing (and often even competing and conflicting) objectives and incentives, standards, and metrics.

The 1990s health maintenance organizations (HMOs) and 2000s accountable care organizations (ACOs) sought to counter the resultant, pervasive, and fundamental structural fragmentation among these different units by attempting to align units' objectives and incentives, standardize metrics, and integrate compatible communication and workflow processes across diverse stakeholders and units. The significant technical and system adoption of EHRs in the 2010s particularly in higher income nations helped accelerate the gradual transition of healthcare systems increasingly into the value-based healthcare system (VHSs), which began their more influential and widespread emergence and expansion in the 2020s. EHR's massive speed, scale, and complexity of data (relative to the traditional paper charts of individual patients locally stored often in physician's clinic and hospital offices) provided a common "language" across system stakeholders to operationalize shared system strategies to begin more concerted and consistent efforts to deliver measurable value for patients and populations. Without value being the ultimate clear, concrete, and common intended output or objective of the healthcare system and the common language of the digitized EHR, it is difficult to see how the future healthcare system can function as an effective unity of its constitutive parts. This "systems thinking" or conceptual framework (of unifying synergistic action) at every level of the healthcare system is required to continually help build and sustain the integrity and thus productivity of the system (Institute of Medicine, 2001). Biologically, cells at the lowest level support the function of organs, which in turn support the function

of the overall organism, as all levels are integrally united in a common operation and objective for the sustained life of the organism. For healthcare systems to function healthily, they must function as systems (which they traditionally, generally, and globally struggle still to do), which thus leads us to consider how might AI accelerate their unification, integration, and realization of their primary objective delivering value-based healthcare equitably for patients and populations.

2.4.2 Digitalization of healthcare: from the digital revolution to Al data infrastructure

The digital transformation or digitalization of healthcare is the technical story of the growing compatibility and mutual influence of the above modern healthcare model and AI data infrastructure. So we will explore the latter here to get to this compatibility, beginning with a conceptual then technological and historical development. The term "structure" refers to its general usage denoting the arrangement of a complex entity's constitutive parts, ordered according to and enabling the achievement of the purpose for which the entity is meant. The derivative concept of an "infrastructure" invokes the traditional physical structures whose networking together supports the sustainable functioning of a community (including telecommunication, electrical, road, water, and sewer systems). Data infrastructure thus is the arrangement of constitutive digital and digital-enabling elements, both technical (software, hardware, networking, and services) and organizational (their associated management, policies, and regulations), that facilitate data production, sharing, consumption, and storage within an organization's larger digital transformation pursuant to its ultimate operating purpose to produce particular goods or services (Hewlett Packard, 2022). Within data infrastructure, cloud storage refers to one of the most dominant tools of digital data storage, typically by multiple computer servers (across multiple physical location with data generated from multiple users) and managed by a hosting organization maintaining secure storage and client-specific on-demand access. Cloud architecture includes the hardware-based server storage networked to the software tools, extending their usability to clients through cloud computing, which pairs storage with ondemand scaling ("vertically" increasing or decreasing utilized storage and computation depending on the real-time needs of the client) and provisioning ("horizontally" widening or narrowing through adapting architecture capacity for client-specific needs for storage and computation services). This value orientation of services significantly reduces the cost while increasing the productivity of organizations who can utilize host capacities without diverting their funds or organizational infrastructure to incorporate those in-house capacities. Data infrastructure thus emphasizes client personalization as the means to the end of enhanced client productivity as the substance of optimized value to the client.

From the standpoint of a technical-historical development, this digital transformation refers to an organization and social economic sector change from the traditional and often manual operation (and the products and processes of those operations) to their digital replacement as part of the Third Industrial Revolution or the Digital Revolution, the general-purpose technological epoch (following the First Revolution of the steam engine driving mechanized factory expansion and the Second Revolution of the electrical commercialization driving mass production) (Schwab, 2021). In each of these revolutions, a new technology catalyzes in often unforeseen ways an exponentially larger economic and societal structural change by accelerating new discoveries, innovations, productivity, applications, and the societal changes to those developments (including in new forms of understanding our world and thus the resultant rules, incentives, and norms of activity and interaction). "Digital" (referring to the digits or discrete numbers of 0 and 1 denoting physical quantities) was applied to the late 1900s industrial revolution ushering in the historical period of the Information Age; during this period, semiconductor and computing technological developments rapidly enabled more rapid, productive, and complex means of communication underlying modern human society (Manuel, 1996).

Digitalization became maybe the most general-purpose technology in history, and its commercialization one of the greatest productivity accelerants. Thus, the organizational and historical development the modern healthcare system model noted above correlates with the intensification of the Information Age, as the greater speed, scale, and complexity of data enable increasing capacities for not only optimized efficiency but also continual system redesign. This growth technically centers on optimization of inputs, processing (with storage and analytics), and outputs (decision-making). The basic structures of VHS organizationally and AI data infrastructure technically share the fundamental workflow similarities of inputs, processing, and outputs. The orientation of such a system model to its ultimate output (value) orders the processing (of healthcare delivery consisting essentially of prevention, diagnosis, and treatment) of healthcare data (of the patient and population-specific data describing their current and projected needs, demands, and expectations as stored, i.e., in EHRs and related financial claims datasets; such data are then analyzed by AI algorithms for retrospective and real-time reporting, in addition to future projection). This vertical model of care delivery exists in Ferlie and Shortell's vertical dimension of the four nested levels of patient, provider, organizational, and political economic. This organizational structure is not simply analogical but also directly operationalized digitally as the data of each four levels inform the horizontal and vertical dimensions of AI's data infrastructure, which increasingly benefits from and is operationalized by AI to handle the explosive growth again of the above data speed, scale, and complexity. The modern healthcare system model of VHS and AI data infrastructure are respectively the organizational and technical sides of the

same coin, that is, healthcare delivery. And it is this healthcare "coin" that is the primary currency of the Information Age. Healthcare accordingly is being digitally transformed historically, while being understood technically as healthcare system's developing data infrastructure (allowing improved prediction and decision-making at the individual patient level by providers and population level by administrators managing and leading the systems).

2.5 Healthcare Al's R&D process

How is this process of digitally transforming VHSs into effective healthcare AI digital infrastructures practically occurring (including for the foreseen future)? This is occurring specifically in six core R&D areas and generally in a redesigned R&D pipeline. Since the healthcare sector is late to the AI game compared to most economic and societal sectors, most of healthcare AI is at the R&D phase. Yet is it still helpful to consider their current usage (to understand present progress) and future directions (to see the likely future next phases as the R&D successes become institutionalized and formalized into platforms for subsequent phases of development and applications).

2.5.1 Al R&D core areas

The main areas of focused AI R&D come down to where much of the contemporary successes are increasingly being demonstrated: prevention and wellness, chronic care management, triage, diagnostics, clinical decision support, and care delivery, which synergistically aim at optimizing population health (through personalized care) through improved innovation, operations, and resultant strategies (Spatharou et al., 2020). Twenty-three of the promising current applications in these areas thus include mobile remote apps (like continuous glucose monitors helping prevent diabetes complications through better chronic care management), e-triage AI tools (with symptom trackers helping patients with particular symptoms determine if they are likely coming from COVID-19, and so require sick patients to present to the ED), diagnostics with clinical decision support (with enhanced integration of EHR-based provider notes and laboratory tests and imaging predicting patients' likelihood of disease progression or recurrence vs. safety to be discharged from a hospital), and care delivery (like with bed management tools predicting surges in sick patients and need for increased provider staff, along with automating tasks for providers throughout peaks and troughs). Consider the R&D case for AI automation. The largest healthcare expenses are staff costs, 70% of clinician time is spent on routine and administrative tasks (particularly open to automation or at least augmentation through standardized work support devices and algorithms), 35% of staff tasks are likely automatable on average (including 48%, 32%, and 30% of work hours automatable for medical equipment preparers, medical assistants, and occupational health professionals

as the top three provider specialties for automation potential), and there is growing deficits in the workforce. Successful augmented automation as AI R&D includes Mayo Clinic's Ambient Warning and Response Evaluation (AWARE) system. AWARE is a clinician-designed, real-time, AI-based clinical decision support EHR dashboard that automates significant portions of critical care providers' chart review of patients by filtering out the approximately 10,000 daily data points per patient down to the 60 most clinically significant and relevant updates that are subsequently displayed according to urgency-and in doing so, AWARE through clinical and randomized controlled studies demonstrated that it improved provider decision-making efficiency, saved providers an average of 1 hour daily on chart review, cut patient mortality odds by over 50%, and reduced individual patient costs by \$43,745 (Ahmed et al., 2011; Pickering et al., 2015; Olchanski et al., 2017). As an example of the increasing fast-tracking or collapse of AI R&D (from design to market scale), Philips, one of the largest multibillion electronic companies globally, acquired AWARE as part of its 2010s refocus on healthcare to commercially scale this R&D product from its initial clinical research design into an internationally available AI product.

2.5.2 AI R&D pipeline design: trustworthy, ethical, and effective Al

The growing number of AI products emerging from these R&D focus areas is increasingly framed according to the R&D pipeline redesign, which we can take as an emblematic and emerging example from Trustworthy deep learning AI Codesign (TAC) (Zicari et al., 2021). The above section on "healthcare AI overview" has already described the promising but still mostly small-scale testing cases of narrowly focused AI products and applications. To reduce the adoption barriers of patient and provider distrust, nontransparent methodologies, insufficient and incomplete datasets, insufficient iterative testing, technically limited applications, and insufficient complementary innovations of such AI R&D products, TAC has reconfigured the basic process of how healthcare AI products are conceived, researched, developed, and scaled. Following the value trend uniting diverse healthcare system stakeholders by orientating them to this common objective, TAC operationally integrates diverse actors (including clinicians, ethicists, and data scientists) at the very beginning of a new potential healthcare AI product. Technically in one of its first success examples, it united clinicians' decision-making diagnosing skin lesions as malignant or benign, ethicists' identification and mitigation of ethical and legal challenges of the AI product and its application, and data scientists' development and application of DL-based AI to effectively achieve the above outcomes within the defined ethical and legal parameters. Trustworthiness of the final product is boosted by codesign of its development and final formulation according to an interdisciplinary, transparent, and end-to-end dialogue of diverse stakeholders optimizing ultimate value for the patient by selecting the best performing AI product comprehensively considered. This new paradigm for healthcare AI R&D may thus provide an increasingly promising present and fruitful future for healthcare AI products. Clinicians help to keep the product at even its initial design phase focused on practical optimization of value-based care for the patient. Data scientists help ensure the product is technically effective and practically easy to use through appropriate best engineering practices in the algorithm design, deployment, and improvement. Ethicists help prevent and mitigate such ethical and societal challenges from AI products including centralization of technical supremacy, unfavorable cost-benefit balance, inequitable societal benefit, biases, data insecurity, cultural insensitivity, interdisciplinary tensions from misaligned incentives (among clinicians, data scientists, and ethicists), and regulatory hurdles. TAC offers a user (patient)centric, team-based, systems thinking, value-orientated R&D paradigm that opens the otherwise seemingly "secretive" AI design, development, and application pipeline to transparent consideration by diverse stakeholders (at the patient, provider, organizational, and political economic healthcare system levels) and across healthcare systems (catalyzing improved competition in value performance among systems, through competition in more trustworthy [i.e., effective, efficient, and equitable] AI-powered system performance from this emerging AI R&D pipeline model).

2.6 Healthcare AI governance and workflow

To design, test, apply, revise, and scale successful healthcare AI from its emerging R&D pipeline, successful governance and management of its workflow is required at all four levels of the AI-accelerated digitalization of the modern healthcare system model. Governance in general is increasingly focused on evolving system needs, including on healthcare AI's workflow specifically.

2.6.1 Healthcare Al governance

The ultimate strategy of system leaders (including executives, managers, and administrators) is the overarching long-term plan to realize the vision of delivering optimal healthcare value for patients and populations, by aligning the system level of diverse providers (in the sociocultural-conditioned political economic ecosystem to this common ultimate objective) operationalized at the level of direct patient care. Tactics are the specific short-term tools and activities that embody and advance the strategic plan. Governance for healthcare AI thus entails the tactical management within the digital infrastructure of the products generated from the AI R&D pipeline, in parallel with the AI workflow and overarching system workflow. The major current and emerging themes system leaders identify for AI governance include improving

- (a) quality, (b) interoperability, (c) scale, (d) change management, (e) security,
- (f) regulation and risk management, (g) recruitment, (h) training, and
- (i) funding (Spatharou et al., 2020):
- (a) quality (through enhanced collaborative, transparent, explainable, and ethical performance allowing diverse stakeholders including patients and providers to understand how, i.e., AI algorithms were developed and can be safely deployed without significant inherent bias that exacerbates technical ineffectiveness or societal inequities; the importance of this theme is underlined by the general perception among providers and patients of data scientists creating AI products without sufficient support once they are deployed, while only 14% of data science start-up leaders prioritize providers and patients in the initial design phase of R&D);
- (b) portability and interoperability (respectively moving and understanding data across multiple cloud, server, or other data systems; this need is heightened by healthcare lagging every major economic sector in digitalization, manifested with widespread and persistent structural barriers among healthcare systems trying to build, share, and improve data systems within and among their organizations without which AI analytics and informed decisions cannot occur):
- (c) scale (through improved resource sharing [including AI systems, products, and datasets] across smaller organizations and lower income communities lacking access to the more expensive and effective AI resources);
- (d) change management (through streamlined, inclusive, collaborative, and paced coordination of clinicians aided in their adoption of AI resources that augment rather than replace them in the activities they help identify as the most clinically meaningful uses for AI resources [i.e., reducing repetitive and routine administrative tasks, or deploying effective clinical decision support tools], at a rate of adoption proportional and acceptable to providers and patients);
- (e) security (through strengthened security of data collection, storage, analytics, and access [including account creation and maintenance, multifactor authentication, proper logging, and data classification] as AI data infrastructure develops with greater number and complexity of networked data servers, clouds, and sources across diverse stakeholders, done in a transparent and robust manner proportional to the sensitive and personal nature of patient's healthcare data; such system duties to the security of patient data need not compromise the technical need for effective AI resources through excessively time and cost-intensive data anonymization and interoperability across diverse healthcare systems with disconnected data infrastructures [which is more challenging in the fragmented US healthcare ecosystem than in Asian or European healthcare ecosystems with more extensive national and integrated systems]);

- (f) regulation and risk management (through consensus-based standardizations of AI conceptual frameworks, cataloging, and practical regulation by centrally recognized and sufficiently empowered regulatory bodies [i.e., clarifying criteria for best practices in AI regulated as a tool/service vs. a product] and risk management [i.e., sufficiently frequent audits of cloud and larger data infrastructure performance, compliance, and security including "compliance by design" for cloud end-to-end orchestration, or the coordinated management of data infrastructure to achieve the stated objectives of user value], in a manner that institutionalizes and automates such regulatory compliance in the very design of AI resource and data infrastructure);
- (g) recruitment (through enhanced healthcare AI-specific training programs in addition to fair and transparent financial incentive structures to recruit and retain competent data scientists, especially given the limited number of such scientists [including data engineers] and the often lower compensation relative to other economic sectors):
- (h) training (through complementary support of the above recruitment measures on the front end of hiring [including expanding existing data science curriculums to include biology, genomics, medicine, and health informatics] and on the back end of continued skill cultivation of healthcare AI data scientists in addition to the interconnected basic AI literature for clinicians [including basic but sufficient education in digital literacy, data architecture, and DL and ML such as through existing continuous medical education requirements] who are involved in collaborative work with these scientists); and
- (i) funding (through adaptation of the above standardized regulatory standards informing fair and transparent pricing for AI products and services enforced within and across systems and states, which is particularly challenging given the widespread regional healthcare pricing differences in those contexts, which only strengthens the need for streamlined, fair, and transparent global reform of healthcare pricing as noted in the previous chapter).

2.6.2 Healthcare AI workflow

To ensure effective governance of effective healthcare AI, the following workflow tactics are critical: (a) objective setting, (b) simplification, (c) standardization. augmentation, (e) embeddedness. (d) (f) interconnectedness, and (g) compliance:

(a) Objective setting: A healthcare system must identify and communicate within and outside its organization a clear vision and derivative strategies to reach it, along with the strategy-informed objectives for healthcare AI operationalizing those strategies to achieve them, along with the related

performance metrics to measure progress (and correct the lack thereof) and thus return on investment (ROI) (Singh et al., 2020). An effective overarching vision (in its medium- and long-term dimensions) can unify a system, inform the resultant abstract strategy (answering "why" system stakeholders should move in the same direction toward the vision), and animate the concrete objectives (answering "how" diverse stakeholders daily can move in the same strategic direction from their diverse specialties and stakeholder positions). The top-cited barrier to successful healthcare AI adoption arises when these objectives are not clear, concrete, aligned, and unifying across diverse system stakeholders: failure in complementary innovations integrating system leaders and data scientists (along with engineers and coders) during the end-to-end R&D process and implementation, including design, development, deployment, and improvement (Moldoveanu, 2019). Leaders may know generally what they want AI to "fix" and scientists may know what AI can do, but the lack of both groups having sufficient overlapping knowledge, incentives, and language often results in impractical asks from leaders and irrelevant answers from scientists (halting any sustained progress in relevant AND effective healthcare AI creation and application). A vision can be "becoming the world's top value-based healthcare system." The strategic plan may be to integrate healthcare AI with a culture of relentless personal focus on the needs of each unique patient within a structure of effective and complementary executive, clinical, support, and AI teams. The objectives could be each of the above teams developing their own AI-based digitalization plans for their existing workflows (including their current strengths and weaknesses achieving their respective performance metrics, barriers to digitalization, and individual champions of that digitalization process), creation of a sufficiently empowered action committee from the above teams to create a unifying and complementary plan, and deployment of the transparent and iterative implementation cycle (like a Plan-Do-Study-Act process) in a gradual phased approach that tests, revises, and scales initiatives in prioritized order across the system (to ensure trustworthy, transparent, effective, relevant, and equitable concrete solutions enacting the abstract strategy) (Taylor et al., 2014).

(b) Simplification: The primary three priorities noted by healthcare system executives to adopt and scale healthcare AI are simplifying and so funding appropriate data governance, sharing, and innovation (Spatharou et al., 2020). By focusing on effective and relevant strategy-informed objectives, systems are attempting to achieve meaningful and sustained successes in their AI-driven digitalization process that captures, processes, stores, shares, and informs optimized strategic, organizational, and clinical decision-making in an affordable and equitable fashion. A healthcare system does not need to build a self-driving car. But they do need to focus their human and financial capital on lean, adaptive, efficient, and scalable

- solutions to the systems' current and emergent challenges to deliver needed and sustained value to their communities (which may start with AI algorithms determining how to sync outpatient clinic and telemedicine visits with local transportation and telecommunication means for their higher utilization patients who have high no-show rates to their appointments).
- (c) Standardization: Healthcare systems must set strategy-informed objectives, while societies must set consensus-informed standards. Generally, the specialty and profession-specific associations of clinicians utilize research, personal experience of thought leaders, and debate to formalize definitions and descriptions of the appropriate diagnoses and treatments for specific patient populations in what is described as the "standard of care." These standards inform payors' pricing for the related treatment and which products and services should be included as part of that treatment ("value" is also defined to an extent according to the degree to which standards are clinically and financially applied appropriately and proportionally to the patient). The introduction, scale, and progress of healthcare AI thus is significantly hampered by the patchwork of loosely defined and often conflicting "standards" of its various components and dimensions, including data sources, access, privacy, quality, digitalization, security, sharing, risk management, and governance in addition to data systems' portability and interoperability. Technically, healthcare AI cannot be improved and financially it cannot be sustained without such standards developed internally by providers, systems, associations, and governing bodies (including professional and political), nor externally by payors and regulators (ensuring compliance, incentivization, reward, and penalties as applicable). The American National Standards Institute (ANSI) in 2020 accredited the first official healthcare AI standard, developed collaboratively with 52 interdisciplinary organizations (ranging from leading healthcare system representatives to technological companies including Amazon, Google, and Philips [a cochair of the working group]) and formalized 11 definitions and traits in addition to 30 concept-specific terms (Anandwala and Cassagnol, 2020). Increasingly more specific and operational standards are expected from this influential baseline. Common standards across diverse systems and societal stakeholders reduce barriers to healthcare AI adoption and development by everyone having the same rules to "play by," by which to ensure appropriate compliance and compensation.
- (d) Augmentation: "Artificial intelligence" may more appropriately be considered "augmented intelligence," as we deploy our human intelligence to design AI as a tool to augment our capacities by being extensions and adaptations to our intelligence. Healthcare AI adoption can improve with system leaders, providers, and patients using AI to augment their existing capacities to achieve their current needs rather than try to replace,

- override, or exclude them from their relevant communities and associated appropriate decision-making. The American Medical Association (AMA) in 2018 adapted their H-480.940 policy advocating explicitly for such healthcare AI as this kind of augmented intelligence, most acutely realized in daily workflows delivering transparent, trustworthy, and safe support for enhanced system and clinician healthcare decision-making for and with their patients (Crigger and Khoury, 2019).
- (e) Embeddedness: Similar to AI productively augmenting rather than inappropriately disrupting existing data workflows, AI products and services must be embedded in existing provider workflows to allow sufficient adoption, enabling it to conveniently generate sufficient value-add without unjustifiable time increases. For instance, the Netherlands' Leiden University Medical Center in 2019 became the first healthcare system to deploy Philips' IntelliSpace AI Workflow Suite (Groves, 2019). This practical end-to-end AI (synced with existing radiologists' workflow) automatically identifies and notifies radiologists of such potential emergencies and significant findings such as intracranial hemorrhages, pulmonary emboli, and nodules, increasing radiologists' interpretation speed of images overall by 26%, while increasing the rate of identifying potential precancerous lung nodules by nearly 20% (Lo et al., 2018; Freedman et al., 2011).
- (f) Interconnectedness: Typically the bigger the data, the better the healthcare AI. And the smaller the healthcare system, the smaller its capacity for effective healthcare AI. There are thus powerful organizational and financial incentives for healthcare systems to collaborate through interconnected healthcare AI to leverage their different capacities for the mutual benefit of their individual systems and the patient populations they serve. The concept of "cooperative competition" ("coopetition") thus emerges as a central promising trait for the future healthcare system model: systems are increasingly seeking to compete on value to attract more patients, while currently competing to attract profitable providers and patient populations yet in ways that periodically require cooperation to meet their individual objectives (Allison and Schmidt, 2020). We can take one of the most prominent arenas of this cooperative competition in AI as an illustrative instance of this. The most powerful AI is mostly being developed in the business and military arms race between US and China corporations and their armed forces. And yet this often fierce competition is bounded by the practical technical necessities of cooperation when neither party is able to independently achieve its primary interests without the help of the other. Such an example is South Korea's Samsung and the US Apple companies which are locked in a fierce economic fight for global smartphone dominance (while Apple's largest supplier of smartphone components is Samsung, which itself benefits significantly from this limited but mutually beneficial cooperation). Similarly, it is unlikely that

healthcare systems either within or across states will be able to individually achieve and sustain dominant market shares over the long term (especially with healthcare AI) without cooperation with other healthcare systems (including more free market economic systems as in the United States). This trend continues amid the growing derivative model from free market capitalism of the IoT-accelerated "sharing economy," powered by peer-to-peer exchange and adaptive joint use of goods and services (like the American Uber or Chinese Didi ride-sharing mobile apps) (Yaraghi and Ravi, 2017), which further supports competitive cooperation in healthcare AI by the development of centers for excellence (US Food and Drug Administration [FDA], 2022; Duke, 2022). Such centers focus on their explicit objectives as fostering partnerships across related stakeholders to capitalize on shared knowledge of best practices in healthcare AI to advance reasonable oversight helping ensure consensus-based standards in equitable safety, effectiveness, and innovation with as little compliance burden as possible.

(g) Compliance: Healthcare AI workflows are ultimately framed and constrained by the primary aim and metric of optimal healthcare system performance (value) within the related regulatory parameters (monitoring different aspects of value). The above points have described systems' necessary operational components of such workflows to advance systems strategically toward their unifying visions delivering healthcare value to their populations (by featuring clear and relevant objectives that inform simplified and standardized design and implementation of effective AI products and services, embedded in existing organizational and clinical workflows, augmenting stakeholders' performance, and enriched by interconnected competitive cooperation with aligned stakeholders and other systems). Value performance is thus the guiding organizational end (ultimately seeking value typically through efficient productivity), while regulations (ultimately seeking safety through mitigating risk) are the guard rails en route to this destination. As noted above, the growth of substantive detail and related consensus on healthcare AI standards increasingly enables appropriate compliance from sufficiently empowered oversight agencies (within healthcare systems, the healthcare sector, and states). The legal dimension of such regulatory parameters relates to liability, as systems and stakeholders can be legally and financially liable for practices and actions that excessively deviate from professionally accepted and legally defined standards. The policy dimension entails licensing, quality control, and professional education for the relevant healthcare AI stakeholders. The financial dimension includes compensation from payors for healthcare AI proportional to often contractually defined prices for specific AI products and services. Given the contemporary early stages for standardization in healthcare AI and the concentration of limited AI talent and power players, such above noted centers for excellence are

increasingly instrumental in helping unify healthcare systems in the development, application, and compliance with consensus-based standards. There is therefore outsized influence upon the global healthcare AI ecosystem from the often political regulatory bodies in states in which businesses and governments have a greater leading role in advancing healthcare AI. This trend is particularly prominent and manifested in the US FDA, the main US regulatory agency for healthcare, which is beginning to categorize and handle AI as a product, particularly ML as a "Software as a Medical Device" (SaMD) within the Food, Drug, and Cosmetic Act (Malek et al., 2022). To obtain initial approval from the FDA for legal distribution, SaMD creators submit to this body their marketing applications detailing the AI's related data and risk, followed by a 510K notification to the FDA Center for Devices and Radiological Health. The majority of these have been for locked or nonadaptive AI algorithms, while a minority can adopt or learn over time (like with DL algorithms that redesign themselves with minimal to absent additional human intervention). The interconnected international expanded in October 2021 when the FDA collaborated with the British Medicines and Healthcare products Regulatory Agency and Health Canada (the Canadian government department for national health policy) to publish the "Guiding Principles," intended to stimulate healthcare AI stakeholders' development of standards for best practices to inform later consensus-based regulation. Various regulatory agencies may additionally be involved in different degrees depending on the type of data involved in the AI (including if the data are personal health information, how and where they are obtained and stored, which organizations execute the above tasks, and where they are located), including the US Federal Trade Commission (FTC) and the European Union (EU) particularly per its General Data Protection Regulation (GDPR) privacy and security law. Both the FTC and GDPR as recently as April 2021 have defined regulatory statues and requirements for healthcare AI stakeholders particularly aimed at optimizing personal privacy and data security through enhanced transparency and bias reduction in algorithms (FTC, 2021; GDPR, 2021).

2.7 Healthcare AI in system design and operation

As healthcare AI's governance and workflow drive healthcare system's value performance upward, while concurrently becoming increasingly embedded deeper into systems (utilizing greater data depth and breadth to further improve performance), there is greater pressure to improve systems' design (which drives further productivity improvement in terms of operations in an iterative cycle informing further redesign). Expounding on the earlier chapter regarding healthcare systems in general, a simplified (but still hopefully helpful) account for the design of modern healthcare systems is that they have historically and organically developed as provider-centric approaches to deploying increasingly complex medical sciences and technologies for increasingly complex patient and populations' needs in a way that financially incentivizes individual-specific volume over value. Despite widespread nuances in such design, virtually all systems struggle with similar challenges of this common background. Such ensuing disease-focused, fragmented, uncoordinated, ineffective, inefficient, and inequitable care fails to deliver sufficient value for patients, accelerating the demand and adoption of "human-centered design" of healthcare AI transforming the future's AI-based healthcare system design (Zimlichman et al., 2021; Clark et al., 2021; Carney, 2021). There are thus shared pressures globally for the design of the future model of healthcare systems to have the inverse traits: AI-driven deliberate and adaptive development of a patient-centric unifying approach to delivering complex healthcare in a personalized manner segmented for related populations in a way that incentivizes personal and population value over volume. It is concurrently a mindset transition from systems reacting to the healthcare ecosystem to one that proactively nourishes its development. Growing evidence thus suggests the future healthcare system model is achieved by reverse-engineered design—starting with value, the interdisciplinary and interlevel collaboration of patients, providers, organizations, and socioculturally contextualized political economic bodies is meant to produce the strategy-informed operations for health-focused, systematic, coordinated, effective, efficient, and equitable care. This AI-catalyzed digital transformation from the current to future design entails certain key developments in the dimensions of (a) organization, (b) providers, (c) collaboration, (d) sustainability, and (e) payment:

(a) Organization: Modern healthcare system design is moving organizationally and educationally away from large hospitals (often academic medical centers where most surgeries and procedures are performed) as the centers of a delivery model that extends out to community hospitals and clinics on the outskirts acting as their referral bases, with most of care delivered institutionally within those hospitals intended to stabilize and rehabilitate as applicable acute medical diseases or conditions. Most physicians are currently trained in such academic medical centers with limited exposure to the majority of disease manifestation and management, leaving much of their formative education occurring in tertiary and quaternary referral centers where more rare and complex care is delivered. The future system design is moving rather toward the reversed model in which the patient is at the center of the system. Academic and large medical centers enrich integrated networks of institutions collaboratively aligned to maximize care delivery as remotely as possible in the various settings of the individual patients (including home, work, and community). The care is personalized through prediction and prevention of acute diseases and

exacerbations of chronic conditions, while maximizing control and management of those chronic conditions throughout the continuum of care and the patient's life (including community-based surgical and procedural management, with physicians-in-training exposed to the full spectrum of this integrated network including those community hospital and clinic settings in collaboration with community-based organizations and stakeholders). Healthcare AI thus informs the strategic, operational, management, and clinical tailoring of personal and population care delivery through better prediction of required system and clinical resources (by enhanced projection of patient population needs) and adaptive, iterative, cyclical value improvement of system care delivery, redesign, and operations. This trend is empirically supported by the 2013-18 reduction of hospital-based acquisitions by healthcare systems by 6%, concurrent with the acquisition increase of postacute care assets by 13%, physician practices by 23%, and outpatient assets by 31% (PricewaterhouseCooper, 2018). And these trends are accelerating with each subsequent year, as evidenced by the volume and value of home health deals alone increasing recently by 30.2% and 64.5% (allowing hospitals to reduce their lengths of stay and readmission rates while increasing their bed turnover rate, ultimately improving healthcare quality for patients and profit for systems).

- (b) Providers: The modern system design centers on physicians delivering complex medical care, which is transitioning into the future design emphasizing multidisciplinary healthcare across complementary specialized roles (in which data scientists and engineers empower patients to remotely monitor and manage their chronic conditions and risk of acute conditions as possible, case managers enable patients to navigate the system to obtain their needed services and products, aided by physical and occupational therapists helping aging and sickening populations maximize independence and functional capacities, supported by nurse practitioners and physician assistances who extend the clinical care of more limited number of physicians, advised by physician specialists when more complex and procedural care is required, and coordinated by primary care physicians aligning the overlapping domains of healthcare by the above providers). This networking of providers is reflected in the top-performing healthcare systems currently who are also the largest by market share: by deploying economies of scale, they are able to effectively profit from enhanced referral patterns servicing the fuller continuum of care without sacrificing the still necessary acute care (while the lowest performing quartile systems have 31% smaller market footprints in the continuum domain and 100% less in the acute) (AHA, 2017).
- (c) Collaboration: The Fourth Industrial Revolution is catalyzing the transition of the medical care-focused design model for modern healthcare systems to a healthcare-focused future design, as the global digital ecosystem is opening up healthcare to an ecosystem perspective (in which

medical provider organizations [with hospital and clinic-based healthcare systems network with medical technology, pharmaceutical, and health insurance organizations] are aligned with tech giants like Amazon and Google, retail pharmacy corporations like Walgreens and Walmart, service provider businesses like Uber and Didi, and social care and education providers to digitally capture and integrate as much of the patient's lived ecosystem in both its local and global dimensions) (Dydra, 2019). Data serve as the common language across these players and partners, valuebased healthcare orientates them in the same direction as the ultimate aim, and an agile and adaptive network structure coordinates their complementary services responsive to patient needs.

- (d) Sustainability: We have already discussed the global consensus on the design shortcomings of contemporary structurally fixed, fee-for-servicebased, provider-centric, medical care-focused healthcare system design. Financial sustainability necessitates the transition to the future design model of AI-driven structurally adaptive, population value—based, patientcentric, health-focused design (from reactionary to active design). The later requires AI-empowered prediction, prevention, and mitigation of disease concurrently with precision medicine personalizing global and national standards of care to the patient level (augmenting clinician decision-making specific to the particular clinical and sociocultural acuity and needs of the individual). There is growing innovative payment models reinforcing and capitalizing on this transition, including outcomes-based, subscription, and annuity pricing (CMS, 2020).
- (e) Payment: Similar to how the Fourth Industrial Revolution is widening the efficiency divide between AI-accelerated and digitally enabled top performers versus traditional and nondigital underperformers, healthcare payment reform is already underway to reward value over volume in the emerging future design model. Such emerging payment innovations incentivize systems to bundle payments at the individual level (i.e., for an entire hospital stay instead of for particular transactions like every laboratory tests), expand payment schemes from the individual to the population (i.e., giving systems a lump sum for an entire population, thus motivating the system to efficiently deliver appropriate healthcare care and minimize waste and care with diminishing health returns), and transition payments to value (rewarding improved quality, outcomes, and cost rather than blindly for increased number of healthcare goods and services irrespective of their benefit, outcomes, or cost for the patient). Nextgeneration (next-gen) managed care organization (MCO) models are quickly sharpening to capitalize on the improved profitability of such payment reforms with 90% of the largest US healthcare payors acquiring care delivery organizations (Clark et al., 2021). These acquisitions are principally in growth-orientated regions like Florida and the Northeast with greater density of disease burdens, value-based market structure (with

integrated community-based care providers delivering enhanced quality for decreased cost), and compressible costs (shunting inappropriately elevated costs to lower-cost settings [i.e., telemedicine for higher utilizer patients who otherwise would have recurrent ED visits]). This trend of complementary horizontal and vertical integration of payor-provider partnerships is additionally notable as the model for future healthcare system design is increasingly featuring integration not only across the traditional system organizations (i.e., hospitals, clinics, and community partners) but also across payors and providers with their dedicated patient populations.

2.8 Front runner for the future's Al-driven healthcare system

To make the above abstract concepts and trends more concrete and informative, let us consider in greater detail by way of conclusion for this chapter the arguable design front runner for the future's AI-driven healthcare system this chapter introduced: Optum. By aggressively pursuing best-in-practices in innovative business models with best-in-practice AI, Optum rapidly grew within a decade of its creation to become simultaneously the world's largest healthcare insurance company and the US's largest physician employer, caring for 80 million patients globally while generating \$101.3 billion in revenue (Mikulic, 2022; Gist, 2022; Haefner, 2019). As noted at the chapter's beginning, its OptumLabs subsidiarity began with Mayo Clinic building what is by 2022 one of the world's largest healthcare datasets (spanning over 200 million patients). It then leveraged these massive data to accelerate its AI-powered clinical and financial insights in an iterative improvement cycle of AI and healthcare system redesign. As its AI algorithms became more powerful in predicting, its integrated organizational structure became more productive, thus feeding back into the workflow of building better algorithms. AI became healthcare intelligence, which became business intelligence, guiding a decade of strategic acquisitions adding new capacities and data, until ultimately becoming the "leader" in next-gen healthcare system design: a single end-toend network of patients, providers (coordinated in a single delivery platform, consisting of a hospital-based MCO linked with an ambulatory care and pharmacy benefit manager), and payor (Byers, 2018). A frantic buying surge of other industry giants of payors buying providers has followed Optum's pioneering path including Humana's Kindred, Cigna's Express Scripts, and Aetna's CVS (Jaspen, 2018). Such AI-informed design integration empowers Optum's scalable platform delivering greater value to patients, enhanced provider competitiveness (buoyed by standardized, repeatable, and adaptively agile end-to-end services better integrated with continually refined strategicinformed operations), and cheaper and more profitable growth for payors

(Perfetti and Cichello, 2017). The sustained profitability surge through its competitive design advantage over healthcare competitors is reflected in Optum outperforming the S&P 500 (the industry-leading stock market index) by 400% in 2018 alone. This vertical integration model for the future's healthcare system model, sharpened by Optum (becoming the biggest payor and the biggest provider), provides a competitive proposal for at least the rough contours of what the future's healthcare system likely will look like.

2.9 The genome of the Al-powered future healthcare system

Like in an AI algorithm, the better quality data inputs, the better quality prediction outputs. And so to approximate the most accurate, precise, and thus actionable vision of the future's healthcare system, we will move from a general sketch of healthcare systems in Chapter 2 and healthcare AI in Chapter 3 to the remaining chapters attempting to decode the "genome" of this system (and thus the adaptive design to which it can give life). This is essentially a clinically and ethically urgent task, not an excessively ambitious or fanciful text. The core argument the remaining chapters will attempt to formulate, formulize, and fortify is that

- (a) AI may allow us to nourish (not simply manufacture or accidentally generate) the emergence of the future healthcare system that can succeed where our past and present systems fail at the personal and population level. AI is the sophisticated solution to finalizing the future's healthcare system design by simplifying it, by refocusing it on its central objective—delivering value-based healthcare to each population globally and each patient individually, as unique and equal persons (and so returning healthcare to its earliest origins serving with the available tools the needs of the sick coming to the healer).
- (b) It can (continue to increasingly) revolutionize healthcare through this simplification, by empowering an adaptive design allowing healthcare systems to think (and so continually adapt, redesign, and re-revolutionize healthcare through greater efficiency and equity).

Like AI, the future healthcare system design need not be a black box. By knowing the data, parameters, and algorithm, we can know how AI works and reasonably what to expect (and direct) it to create. Similarly, by knowing the components, limitations, and strategy-based operations, we can know (at least to some informative degree of accuracy and precision) how healthcare systems are developing into the model for the future, and how they can be nudged into the optimal direction of the value patients and populations need (among what can reasonably be delivered). The previous chapter introduced what healthcare systems and AI are. The previous sections set the stage for the scope of this next phase of the argument by introducing healthcare's digitalization and the

resultant healthcare AI's R&D, governance, workflow, design, operations, and emblematic power player. This allows us in the subsequent chapters to pivot to the concrete details defining, exploring, and applying how AI is transforming the future's healthcare system in its technical domains and societal context (within the digital health ecosystem framed by and influencing patient safety and security, politics, economics, ethics, and the globalized dimension of healthcare systems). The technical domains will consider precision medicine (including personalized risk stratification, prevention, diagnosis, prognosis, treatment, and palliation) and public or population health (including population modeling, pandemics, poverty, climate change, and wars and geopolitical conflicts), integrated with healthcare system delivery (with AI-informed adaptive system design that includes structural streamlining, telehealth, and digital engagement [including provider-patient interactions and mobile monitoring). So let us move now to the concrete genome or structure of human-centered AI design driving the future's human-centered healthcare AI system design, efficient enough to be equitable.

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Al + precision medicine: data science and multiomics

3.1 Precision versus personalized medicine

3.1.1 Conceptual distinction

Precision medicine or PrMed, which will be discussed in this chapter, and population and public health or PubHealth, which will be discussed in the next chapter, can be considered as the two poles on the one spectrum of the future healthcare system, connected by the AI "bridge." Before we get to this bridge and PubHealth, we will first consider an overview of PrMed before digging deeper into its historical development, current operations, emerging trends, and expected trajectory (particularly with the AI-accelerated patient-level omics integration with clinical care [emphasizing risk stratification, prevention, diagnosis, prognosis, treatment, and palliation] and system-level integration with human and material resource management).

PrMed generally refers to the customization of treatment for an individual patient based on her/his unique situation (both in the macrodimension clinically and socially/environmentally [including family health and personal health, lifestyle, and geographic data] and microdimension [including genetically and epigenetically]) (Schleidgen et al., 2013). The US National Research Council in its influential 2008 definition emphasized that this tailoring occurs by more accurately and exactly classifying individuals into increasingly detailed subpopulations according to their likelihood of developing a certain disease or responding to a particular treatment (thus maximizing clinical effectiveness while minimizing avoidable harm and cost) (National Research Council, 2011). In line with compatible global trends, the Council explicitly chose "precision medicine" over the older term of "personalized medicine" to reduce the possible misperception that preventive and treatment interventions were created and deployed specific to each individual. There are prominent critics within the global healthcare community that do advocate for personalized medicine including "one-person trials" or "N-of-1 trials" (with N traditionally representing the number of subjects in a study), in which medications are designed, created, and utilized at the most personalized and precise level—for one individual at a time (Schork, 2015).

3.1.2 Genomic matching with umbrella, basket, and N-of-1 trials

Such criticism of the current performance of most healthcare systems is that they focus on "imprecision medicine," providing patients for instance with pharmaceuticals that only help up to 1 in 25 patients, and may have disproportionate harm to ethnic minorities given their historic underrepresentation in clinical trials and studies. "Personalized" is already how providers essentially (at least in theory should) care for patients. Patients come to us as clinicians with their concerns and complaints, and then we attempt to classify the constellation of their signs and symptoms with the most accurate and precise diagnosis, utilize the most probable effective prevention and treatment specific to the unique patient, and then modify that regiment based on each patient's individual response. Yet there must be studies of pharmaceuticals before they can be clinically utilized and guidelines defining standards of care (that are for the most part "individual blind" but rather "population focused"). The medical community widely acknowledges the rampant and sizable inefficiency of time and resource of the biomedical R&D process (i.e., with Phase 3 trials requiring often thousands of patients usually with little baseline information on genetics and environment that make certain individuals more or less likely to respond to the analyzed prevention or treatment measures). As part of an emerging trend of innovation in study design, the NCI-MATCH (National Cancer Institute Molecular Analysis for Therapy Choice) trial from the US National Institutes of Health (NIH) is a pioneering PrMed study that carefully selects patients for inclusion and assigns them to treatment based on their cancer genetics (matching the treatment as precisely as possible to their actual disease), rather than the traditional approach of treating cancers based on the primary organ from which they developed (Flaherty et al., 2020). Interim analysis demonstrated that this more exact matching of treatment and individual can be efficiently accomplished even in a large national network trial. The related design innovation of an "umbrella trial" in contrast tests multiple treatments based on multiple genomic or molecular traits of the tumor for patients who share a similar tumor (by primary anatomic site of origin), similar to "basket trial" which also tests multiple treatments for patients but based on a specific biomarker across multiple tumor types (Chen et al., 2019).

And yet even precision treatments may not be precise enough if they make it successfully past such rigorous trials. Emblematically, the drug vemurafenib is approved for late-state melanoma (skin cancer) but specifically those cases with the BRAF (V600E) genetic mutation may still fail, as a 2019 basket trial using the AI ML technique of orthogonal partial least squares demonstrated that tumor upregulation of ErbB protein receptors increases resistance to the drug (Carroll et al., 2019). How precise does a trial or drug need to be to be sufficiently personalized and thus effective? Growing proof-of-concept examples suggest that PrMed may not only increasingly approach personalized medication through N-of-1 trials but also be pragmatically effective even in less complex diseases. A seminal 2010 Australian study on three of the more common and difficult-to-treat diseases (osteoarthritis, chronic neuropathic pain, and attention-deficit/hyperactivity disorder [ADHD]) showed how three N-of-1 trials were successfully run in parallel while ultimately reducing patient costs (through decreased use of ineffective treatment and increased medical consultations) and time for optimal drug identification (Scuffham et al., 2010). While N-of-1 trials collapsing precision more into personalized medicine is likely less practical (and ethical) for PubHealth (i.e., optimal pandemic mitigation techniques), it may be more feasible and preferable for rare and multidrug-resistant diseases or in early clinical trial phases. The growing AIaccelerated Big Data trends in modern healthcare systems (that are projected to facilitate the transformation of routine clinical care into concurrent effective and efficient N-of-1 trials) include the following: digital health (with relatively inexpensive remote sensing devices including the Apple Watch and CGMs), increased funders and government pressure globally for more individualized treatment, and translational omics (the biological sciences ending in -omics including genomics, transcriptomics, proteomics, and metabolomics, which together seek to causatively describe the components and relationships of molecules enabling an organism's structure, function, and dynamics) (Schork, 2015; US FDA, 2013; Institute of Medicine, 2012). Nonetheless, significant cost (tailoring treatment) and regulatory barriers (moving away from commonly accepted traditional trial designs) are and likely will remain longterm barriers to more precise PrMed for the foreseeable future. Such barriers may be overcome particularly if such a more personalized approach to PrMed (accelerated by AI) can demonstrate increasing effectiveness and efficiency (particularly by reducing harm and cost from ineffective treatment).

3.2 Precision medicine's historical development

Given the generally and globally accepted preference of PrMed over personalized medicine, its wider current prevalence and pragmatism, and persistent openness to a more personalized later development, we will from here on focus on PrMed unless specified otherwise. PrMed's early modern historical trends can be traced to the early 1800s Great Britain to what has since been a generally criticized application of social Darwinism for medical statistics, as Charles Darwin's cousin (Francis Galton) and the founder of modern statistics (Galton's protégé, Karl Pearson) developed pioneering statistical tools to optimize human health (Gillham, 2001). While acknowledging their significant mathematical and medical advances, their social application of such statistics for eugenics has been widely critiqued for its support of such practices as selective breeding of "preferred" groups and reduction of others (particularly lower income and racial minority individuals) including through state-mandated sterilization and termination (Reilly, 2015). The 1900s witnessed the medical community's broad move away from eugenics-focused

PrMed to large cohort studies and finally to pharmacogenetics, as increasing genetic insights advanced pharmaceutical development for more tailored treatment of patients. This trend was accelerated following the 2003 completion of the US NIH-led Human Genome Project (HGP), the world's first global biological collaboration that sought to sequence and map physically and functionally the genes of the human genome (or the 23 chromosomal pairs encoding the DNA instructions determining human development and function biologically) (Green et al., 2015; Collins and McKusick, 2001). Early PrMed fueled by the HGP allowed the production and widespread use of the genetic-specific cancer drugs of Gleevec (imatinib), Erbitux (cetuximab), and Herceptin (trastuzumab) (National Research Council, 2011).

The 2010s onward with the surge of electronic health records (EHRs) and healthcare AI then opened a new digital front in PrMed to use large datasets (including environmental, social, clinical, biomarker, and genetic data) to predict, prevent, and treat disease at the individual level (Snyder, 2016, p. 1). Such digital-driven large-scale PrMed efforts include China's Kadoorie Biobank, the UK Biobank, and the US All of Us, with the latest being the largest to date PrMed comprehensive dataset (featuring cloud-based biological, environmental, and lifestyle data from diverse patients including racial minorities who are typically underrepresented in medical research) (Govern, 2022). This PrMed approach to modern healthcare helps to reframe it by operationalizing statistical and societal diversity for more effective and equitable healthcare delivery. The large sample size allows greater statistical power to identify novel disease patterns within individuals at the intersection of environment, lifestyle, and biology (including health, genetics, and biomarkers), thus empowering more sophisticated predictions for individuals (NIH, 2018). EHRs, mobile remote-sensing data (i.e., from such devices as Apple Watches), blood, urine, saliva, genomes, physical measurements, and survey-reported lifestyle aspects among other data sources from over one million diverse subjects give unprecedented breadth and depth computationally to capture a more complete and accurate health picture concurrently at the population and patient levels. Secondarily, more equitable representation societally (as seen with over 51% of the All of Us included individuals from racial and ethnic minorities) makes possible more effective and fair medical advances (considering how up to this point, approximately 90% of all largescale genomic studies have been on patients from European descent, leaving most of the modern medicines developed with a skewed genetic understanding of the world's patients) (Govern, 2022; Dishman, 2019).

Such developments manifest the increasing AI-accelerated role of PrMed in improving clinical effectiveness and social inequities in modern healthcare. Now it should be noted that the medical sciences within healthcare historically have focused on tailoring general principles to the specifics of the patient from its earliest to its current practice. The emergence of PrMed as a more distinct and defined healthcare trend and era within modern healthcare thus highlights

the fundamental reshaping of contemporary medical practice with its pharmacogenetic and even more so the AI-driven digitalization applications, opening new capacities and trajectories for personalized care specifically (thus remaking the face and core of modern healthcare generally to deliver on its original objective). As such, contemporary PrMed provides a microcosm of emerging modern medicine and a telescope into its future. It qualitatively shares medicine's central objective of effectively treating the particular patient using general biological and statistical principles, but it quantitatively focuses on this personalization with greater fundamental and intense focus and operation (which AI and Big Data are key to achieving). And AI is "unlocking" the potential for this Big Data (characterized by its defining dimensions of unprecedented volume, velocity, and variety of digitized information [or Big Data's "3Vs"], exploding with IoT), which synergistically drives the Digital Revolution of modern societies and industries; AI makes analytics on powerful datasets and streams more sufficiently effective and efficient to help drive better decisions clinically (at a patient level) and organizationally (at a system level) (Sinur, 2019). What would have happened if humanity never crossed the seas which cover nearly 80% of the planet? Or what if you only used 20% of the information about your finances like what is in your bank account to decide future financial decisions such as if you can afford to buy a larger purchase? What if physicians only used 20% of the information about a patient to diagnose and treat her/him? Yet 20% is how much not only in healthcare systems but also in other economic sectors is currently used on average to drive decisions, leaving AI to harness the latent 80% of Big Data in those related organizations' digital ecosystems (needing to be digitized, centralized, standardized, and analyzed at a scale and speed that increasingly requires AI given the technical demands exceeding human capacity). Medicine began walking into modernity with statistics, running with pharmacogenetics, and flying with AI-enabled digitalization in a transition catalyzed, captured, and conceptualized with the focused movement within healthcare of emerging PrMed.

3.3 Precision medicine versus public health: fighting for healthcare's future

The promise of PrMed comes with its perils, playing out in the first 2 decades of the 21st century as a tug-of-war with PubHealth for healthcare's future. The US President Barak Obama when he launched the Precision Medicine Initiative (from which All of Us was born) hailed PrMed as "one of the greatest opportunities for new medical breakthroughs that we have ever seen" (Obama, 2015). The potential has already been increasingly realized for numerous medical advances, though there is mounting caution about the actual potential for PrMed and its overemphasis at the expense of PubHealth. Personalized treatment is key, but it has thus far often produced minimal gains for limited numbers of patients at high costs—while significantly more effective, affordable, and equitable population-wide preventive measures with greater societal benefit for the burden of diseases have suffered from underfunding and research attention (Bayer and Galea, 2015). During the 2010s with the Big Data—fueled surge of PrMed projects and funding, the proportion of NIH-funded PubHealth programs plummeted by 90%, suggesting that PrMed is being advanced at the expense rather than as a complement to PubHealth, thus reducing current and future healthcare benefit for patients and populations on average. Concurrently, PrMed research publications have grown at 500% in the first 2 decades of the 21st century, while PubHealth publications remained static at 0.1% of overall research (Cohen, 2019).

There are growing structural and programmatic interventions within the health system ecosystem to bridge this divide. AI and Big Data together can complementarily unite PrMed and PubHealth, as with the CDC's Office of Genomics and Precision Public Health personalizing care and resources concurrently at the patient and population level by leveraging strategies and insights from each. This pragmatic collaborative rather than competitive relationship within and across healthcare systems is accentuated by the limited maturity of more costly and less effective (though still promising) PrMed programs, as 88% of systems report their programs are not yet fully mature and nearly one in three system do not even have PrMed programs (Cohen, 2019). Concurrent with these structural advances are those in emerging biomedical research paradigms driven by Big Data. The largest study to date of US twins spanning 45 million patients (helping differentiate genetic vs. environmental [including economic, climate, and air quality] predictors of health outcomes) demonstrated across 560 common diseases that genetics contributes to 40.18% of them while the environment affects 24.64% (Lakhani et al., 2019). This AI-based digitalization of PrMed within healthcare Big Data (HealthBD) thus is increasingly advancing not only PrMed but also current and future healthcare by concurrently and complementarily strengthening PubHealth.

It is not deciding whether to choose the genetic code or the zip code to treat patients, but rather choosing to deliver optimal value to patients by using both. As physicians sometimes need medicines and other times a scalpel depending on the patient's needs, healthcare systems are seeking to better develop and deploy PrMed and PubHealth as the operational pillars for healthcare delivery in the emerging future healthcare system model (guided by AI-leveraged Big Data guiding the synergistic relationship of these pillars). PrMed and Pub-Health become the two columns or organizational "chromatids" of the future healthcare system's "chromosome" giving and guiding the birth of a new living model of healthcare, held together by the "base pairs" of AI-enabled HealthBD connecting both chromatids to ultimately transcribe value for the patient. As scientific competence and humanistic compassion are complementarily critical in a healthcare system's central existential encounter (between the physician/clinician delivering healthcare face to face with the

patient as a person), PrMed's effectiveness and PubHealth's efficiency are increasingly united therefore through AI-driven HealthBD to accelerate the journey toward value-based healthcare's future. So we will now pivot to how AI-based digitalization helps concretely advance PrMed in its collaborative role in this projected (and needed) future for healthcare systems: not as PrMed versus PubHealth for healthcare's future, but rather as PrMed + PubHealth = (via AI) healthcare's future. We will focus on the PrMed part of the equation in the subsequent sections and PubHealth in the following chapter.

3.4 Al + healthcare Big Data = precision medicine: Big Data, chaos theory, and AI overfitting

3.4.1 Healthcare Big Data: clinical and organizational structures

The 20th-century evolution of medical statistics and computing power paved the way for the contemporary data analytic and storage dimensions that now characterize PrMed (Phillips, 2020). Following WWII, the NIH became the world's top funder of not only biomedical research (including biostatistics methodologies) but also research digitalization (including computers for electronic storage and analysis of research data), facilitating the institutionalization through universities and research centers of this dual capacity in modern biomedical research through the pressure of funding mechanisms. Consider the NIH's Framingham Heart Study launched in 1948 to primarily define the rate of cardiovascular disease (CVD) in a population. A decade of statistical methodology advances allowed clinical, biomarker, and behavior traits to be incorporated into prediction models for an individual's risk of developing CVD. Moving from what is to what likely will be, the NIH statisticians' work in such observational analytics led to the later formalization of causal statistics in addition to randomized clinical trial designs in parallel with nonobservational analytics (Ellenberg et al., 1994). From population-level disease prevalence to patient-level disease prediction, the growing biomedical data storage and sophisticated analytics allow the fine-tuning of pati ent-level prevention and treatment to reduce such diseases' morbidity and mortality. As the data got bigger and the statistics smarter, predictions (and the treatments they informed) became more precise, effective, and efficient.

Following PrMed's early statistical era in the 1800s, its post-WWII biomedical study era, and early 2000s HGP-upgraded pharmacogenetic era, what characterizes its post-2010s AI-based HealthBD era? If the first few thousand patients in Framingham in the 1940s gave unprecedented health insights, what will the 45 million subjects from Lakhani et al. mean for the 2020s and onward? Ginsburg and Phillips propose that this AI-accelerated Big Data will move PrMed (and healthcare more broadly) "from science to value" with data science (focused on AI and its Big Data) uniting the platforms of PrMed and digital health (Ginsburg and Phillips, 2018). This current phase digital

revolution of PrMed has both clinical and organizational dimensions (at the point of care between providers and patients and at the system level managing organizational strategies and resources in a larger open societal system, affecting healthcare systems in their sociocultural-conditioned political economic environment). HealthBD describes the part of healthcare systems and their larger societies' digital ecosystem most related to healthcare delivery that can be collected, stored, analyzed, and acted upon pursuant to the strategies and tactics of healthcare systems to ultimately deliver optimal healthcare value. PrMed's data ecosystem centers on the central patient—clinician relationship that digitally is translated into the EHR (detailing patient phenotypes or manifestations of signs, symptoms, laboratory and imaging findings, and the overarching diagnoses [medical history] in addition to the patient's omics profile, exposures to particular disease risk factors, family history, and health outcomes) (Aronson et al., 2015). This horizontal data pipeline is increasingly infused with the adjunct information from digital health (with telemedicine and remote sensor devices) and data science (including cloud infrastructure linking the larger societal and global data ecosystem) to drive the iterative patient- and population-level health outcome optimization (with that outcome data informing back the initial steps again with clinicians [in collaboration with the supportive and executive system staff and the larger device, pharmaceutical, regulatory, and funding bodies]) interacting with those and future patient and populations (Institute of Medicine, 2015). The data science platform thus opens a vertical dimension to this pipeline by connecting clinical data to organizational data (Secinaro et al., 2021).

The latter system management data include supply chains that when paired with predictive algorithms allow "just-in-time supply systems" to improve logistical and workflow efficiency (including reducing storage and management costs by better fitting medication supply to timely impending patient needs, while improving drug discovery, approval, and deployment time and costs) (Fleming, 2018; Chakradhar, 2017). Rural health inequities may additionally be reduced through this AI-enabled HealthBD with improved diagnostics (including swallowable endoscopy capsules with remote AI sensing for gastrointestinal [GI] cancers, malarial diagnostic models based on automated Giemsa-stained peripheral blood samples, acute leukemia prediction models based on bone marrow images, and clinical decision-making tools for peripheral neuropathies) in addition to staff training on this technology (Guo and Li, 2018). Such AI clinical benefit at the patient level can be better sustained, scaled, and institutionalized into existing healthcare system workflows through a "multilevel medical AI service network," consisting of the frontline or basic level at the point of care for the above technologies particularly in rural and underserved communities, supported through the regional or middle level centers, and coordinated through national or top-level development centers.

The clinical dimension of the HealthBD structure prominently features EHRs. Given the growing prevalence of EHRs throughout diverse healthcare systems and regions globally, there is increased research and organizational interest in improving healthcare value by AI-guided utilization of the EHRbased contribution to the larger HealthBD infrastructure within and among healthcare systems. Such EHRs provide a data-rich and efficient target for operationalizing this data source by integrating it with systems' larger data infrastructures. Where the healthcare system is, there the healthcare data are (upon which the system runs). This makes the primary task for the EHR's HealthBD application the optimization of its portability and interoperability so it can communicate with the larger data infrastructure and so be analyzed and acted upon (rather than having to be collected, which historically has been the primary barrier to more efficient and effective healthcare data-driven clinical and organizational decisions). In systems beginning with their digitalization and moving toward AI deployment, these EHRs can often be the first major data source and structure for their HealthBD infrastructure. "Deep EHR learning" is emerging within this trend as the intersection of HealthBD and AI analytics for practical clinical informatics programs that have greater performance and efficiency (particularly in reduced time and resources required for feature [programming] engineering and data preprocessing) than the older traditional ML and statistical methodologies (Shickel et al., 2018). Aside from the individual clinical application, the already demonstrated population-level organizational applications of this deep EHR learning include predicting data heterogeneity (variability) within and across systems (to allow compatibility streamlining for data aggregation and analytics across devices, clinics, and hospitals), improving resource utilization prediction (to better staff and equip by improved prediction of disease development, hospital readmissions, heart failure admissions, and short-term suicide risk stratification), and defining and improving transparent benchmarks for continuous quality improvement of system services (Miotto et al., 2016; Nguyen et al., 2017; Choi et al., 2016; Tran et al., 2015). Miotto et al. in particular demonstrated a powerful deep learning (DL) application using a large EHR dataset of 700,000 patients that outperformed competing methods to predict 78 diseases (with specific cancers, severe diabetes, and schizophrenia being among the best predicted diseases). Such an AI algorithm allows a clinically, time-, and costefficient approach for systems to better tailor their provider workforce (in number and specialty) based on a better understanding of communities with evolving health needs before those needs even arise (especially considering how recruiting, training, and transferring clinician specialties across the clinics and hospitals in healthcare systems can be a costly multiyear process).

3.4.2 Healthcare AI analytics: model fit conceptual overview

Now to better understand the accelerant role of AI modeling in PrMed, consider an illuminative example from mathematics' chaos theory articulated by the butterfly effect. Can a Brazilian butterfly flapping its wings cause a

Texas tornado over 5000 miles away, or in other words, can deterministic chaos accurately describe how seeming unpredictable and random events can occur in a general system seemingly determined by objective material laws of operation according to classical physics (Augustyn et al., 2021)? The Massachusetts Institute of Technology professor, Edward Lorenz, proposed this mathematical model in a way that "accidently" led to the formal creation of chaos theory as a way to study how prior conditions can be used to predict short-term outcomes, while demonstrating the challenge of predicting longterm outcomes, which becomes more difficult with an increasing complexity of factors affecting them—in a complicated but not random fashion (Dizikes, 2011). Lorenz mathematically proposed in his seemingly humble and esoteric (and initially minimally cited) 1963 scientific paper, "Deterministic Nonperiodic Flow," the above principle through computer simulations predicting weather patterns. Since then, there has been a profound paradigm tornado ripping its way initially through meteorology and then through such diverse fields as biology and geology. Lorenz helped fundamentally break open modern science's previous nice, neat, and deterministic Newtonian mechanical system of the "clockwork universe" of nature described conceptually as reliably predictable—if you just knew enough of the past and present factors, you would foresee accurately the future. Yet Lorenz successfully demonstrated quantitatively how his butterfly effect limited accurate weather predictions to just 2 weeks out from the present (beyond which, i.e., even small errors of imprecise storm location or clouds could, respectively, double in magnitude by 1 and 3 days). Lorenz discovered this nonlinearity trait of weather derived from such wind-induced uneven horizontal movement of moisture, heat, and other atmospheric traits. Weather thus operates in a chaotic nonlinear system (not arranged in a straight line) according to Lorenz. Biologically, you cannot accurately predict two mouse populations over 10 decades in a linear fashion if one starts with 20 and the other 22 mice—they will empirically both have 2000 on average as chaotic factors like limited resources, infection, and death will have nonlinear effect on population outcomes. A prediction model for outcomes in general therefore must be run multiple times with as much data as possible to produce a more accurate forecasting (a practical analytic necessity Lorenz facilitated in numerous current disciplines, including meteorology producing more accurate and reliable "consensus" forecast of weather or in a spaghetti model of a hurricanes' likely paths by utilizing larger data collection and more complex modeling).

Lorenz's more modest modern analytic approach catalyzed significantly more empirically precise predictions from diverse disciplines as scientists sought to better account for such chaos. The statistical and data science corollary of this phenomenon may be the "missing variable bias," supporting the traditional maxim that all statistical models (attempting to predict the future by knowing past factors) are wrong, but some are useful. Modern statistical and their newer related AI models thus seek on average a careful balance to

optimize utility: building a prediction model with as many of the necessary predictors as possible to thus avoid underfitting (knowing no dataset will ever contain all the necessary and sufficient predictors that "determine" future events) while still avoiding overfitting (IBM, 2022). If a predictive or statistical model "fits" perfectly against the training data (of potential past predictors of future events), then its external validity or generalization is limited for new datasets. The model can tell you everything you want to know in the training dataset, but not for any other similar data because it matched even the "noise" or less relevant factors in the original training data to the model. Therefore, in data science, we typically split a dataset into training and test sets so the model built in the training set can be checked off the test set, increasing the likelihood we can arrive at the optimum model that avoids the high bias, training error, and test error of an underfit model on one hand, in addition to the high variance and test error with low training error of an overfit model (the training set is often additionally split into a subtraining set and validation set so the model can be trained or created and then evaluated and improved [including choosing the best performing model among diverse model options] using the validation set before confirming the results on the test set [with the training and validation datasets often using the same internal data which are then compared to an external test set]). You want to arrive at the "sweet spot" of an optimal model after enough (but not too many) iterations of the training and validation sets, where there will be minimized error for the training and validation sets, beyond which point, error continues to drop for the training set but asymptotically increases for the validation set (like a "U" shape that you realize once you start from the trough and start climbing back to the right side of that shape's peak—we have to rather stay at the bottom of that "U" before error starts rising again). Even a 2020 empirical study on quantum mechanics which argues against the butterfly effect (as one of the strongest arguments against it thus far) appears to support it by demonstrating quantum entanglement (joining two particles through space and time to operate as one unit to remain in the same state) and facilitating "self-healing" reality, as altered or damaged quantum information or qubits were recovered through its unaltered or undamaged correlated bits of other information (i.e., the butterfly and tornado can be entangled nonlinearly) (Yan and Sinitsyn, 2020). To avoid overfitting, we must avoid excessive iterations and complexity of the model. The illusionary seduction of omniscient in data science must practically be tempered by the pragmatic necessity of just enough ignorance to produce the most accurately and precisely fit models. Like a clinician waiting on a patient's lab results or a healthcare executive waiting on market trend data, the optimal "fit" for clinical and organizational decisions in healthcare systems requires enough time and data to make the best decision at the time (beyond which point greater harm from indecision can occur even if there is greater data to take more "informed" action if you wait longer).

3.4.3 Healthcare AI analytics: AI-HealthSIPs and model-informed decisions

So how can optimal modeling informed analogically by chaos theory help us understand the role of AI analytics in PrMed? This central tenant of AI-based PrMed provides a type of analytic portability and interoperability. Optimal PrMed, both in the clinical and organizational dimensions, increasingly requires the agile analytic ability to scale up and down (from populations to individuals) and zoom horizontally (out and in according to the required system stakeholders and providers) with the complexity of the model to determine the AI-enabled healthcare system inflexion points (AI-HealthSIPs) in prevention, treatment, and system management and thus how systems can operationalize those interventions optimally. Like in calculus where the inflexion point is where a mathematical function changes concavity (or a Ushape changes from going "down" to going "up"), these AI-HealthSIPs help clinicians and administrators know where the most benefit can be produced for the least harm where the inflexion occurs. Like clinical inflexion points in the critical care unit, as a physician I have to often give just enough fluids to a patient with severe heart failure presenting to the hospital with septic shock from a life-threatening pneumonia infection. Too much fluids can exceed their heart and lungs' capacities and force them into acute respiratory failure requiring intubation and mechanical ventilation. But too little fluids can prolong the shock and the related mortality even with intravenous pressor medications. Analogically, an AI-HealthSIP is the "Goldilocks" point where the most net benefit is produced through optimal system response (clinically and organizationally). At this AI-HealthSIP, interventions are tailored as much as possible to the individual based on what works best for the most finely classified subpopulation to which she/he can be matched (responding or intervening with as much intensity with the most appropriate type of intervention as the individual can derive the most benefit from, before the risk and harm from any further intensity or type of intervention begin producing net harm rather than net benefit).

Consider arrhythmia-caused sudden cardiac death (SCD), one of the most sensitive downstream markers of healthcare inequities and difficult to prevent diseases (Monlezun et al., 2021). Lower income racial minorities bear a significantly disproportionate burden of disease compared to higher income racial majority populations, as SCD often results in the former group as the first manifestation of underlying chronically uncontrolled CVD (which higher income racial majorities have lower incidences of given their higher healthcare system access to manage their CVD). Thus families may often find out that their poor loved ones often are much sicker than they believed when they suddenly collapse with a heart that simply stops after too many years of uncontrolled diabetes and hypertension clogging the coronary arteries around the heart, while richer patients usually are more able to see clinicians to have their

conditions diagnosed, treated, and controlled before they progress to catastrophic threat to life. Emerging AI analytic techniques in PrMed integrating ML and geospatial monitoring help pinpoint the hardest hit vulnerable patients and communities to thus guide for instance the deployment of healthcare system resources (to more accurately and aggressively risk stratify subpopulations of patients and focus on more effective and lower cost prevention, particularly given the approximately SCD's 70% mortality rate largely static even in a high-income nation for over 3 decades, with only costly acute and rehabilitation care available for the few survivors). It is one thing for physicians to see a patient in clinic and conceptualize a rough personal risk of SCD to guide changes in medication treatment such as with more aggressive cardiac evaluation for progressive shortness of breath (potentially as an early warning sign of congestive heart failure as a precursor to progressive heart failure and eventual SCD). It is quite another to have the above AI-based approach (that considers the nonlinear development of SCD which prompted the search for environmental factors such as income and neighborhood location) to better understand where those higher risk social networks of patients live to better inform for instance if a healthcare system should open more lower cost clinics in those neighborhoods to increase healthcare access and effective prevention.

In parallel with this organizational dimension of AI analytics in PrMed, a 2022 study using a hybrid analytic approach integrating DL and traditional statistical survival analysis across a multicenter dataset using only raw cardiac images from contrast-enhanced cardiac magnetic resonance images (MRIs) not only outperformed traditional survival models (built using clinical predictors) but also generated accurate longitudinal predictions of SCD up to 10 years out (Popescu et al., 2022). Such research has immediate operational utility to automatically screen and personalize more aggressive prevention measures for patients with less time and cost (by not only potentially reducing the heavy clinical and financial burden of SCD but also reducing the use of suboptimal measures and medical consultations). Such measures notably can be deployed even in lower resource healthcare systems that may have less resources for more advanced or higher number of clinical specialties, as such enhanced diagnostics can be automated as part of the treatment algorithms and included images integrated with lower cost primary care providers (PCPs). Such AI-HealthSIPs can be more quickly, accurately, and precisely identified and acted upon to bend the disease and cost trajectory for patients, populations, and their healthcare systems—while enhancing health equity.

3.4.4 AI-HealthBD: impact on future healthcare system design

When the clinical and organizational dimensions of AI analytics help unlock the value potential for HealthBD (in AI-HealthBD), an interesting trajectory opens for future healthcare systems' design. We have previously introduced the growing proposal that AI can bridge the two poles of PrMed and PubHealth on the healthcare spectrum by optimally fitting prediction models to identify actionable AI-HealthSIPs (maximizing benefit and minimizing harm/cost). But what happens when PrMed is done at the individual level for more and more patients until it reaches critical mass at a population level? Does AI compress PrMed and PubHealth into a single entity of future's healthcare that agilely oscillates between both platforms, emphasizing the complementary individual or population dimension (along with the clinical and organizational dimensions) depending on the real-time changing requirements of delivering optimal individual and population healthcare value? We considered in the above subsection how HealthBD increasingly connects healthcare systems' data to increasingly accessible and intelligible networks of dense, interconnected, and interdependent data that are both clinical and organizational (in addition to the interconnected larger societal and political economic data ecosystem globally). We also surveyed AI analytic advances that operationalize that data to produce actionable clinical and organizational interventions. AI in this emerging design of the future healthcare system may thus be serving less as a bridge (connecting the separate submodels of older statistical and nondigital data-based PrMed and PubHealth) and increasingly more as a prism of an increasingly integrated model of PrMed-PubHealth or AI Health—as the prism changes the angle, you can see more of its PrMed aspect or more of its PubHealth aspect, which are intrinsically united (digitally and organizationally) in their respective interdependent diversity.

These aspects become more seamless, integrated, interdisciplinary, and complementary answers to the separate question of "How to care for the unique patient?" and "How to care for the common population?" Scientifically and existentially, the answer in a sense is that the individual is the community and the community is the individual. AI Health is not having to choose between taking care of one or the other. I remember the first patient I cared for with an ST-segment elevation myocardial infarction (STEMI) or heart attack who came into our hospital with a cardiac arrest. The coronary vessels on the heart's surface that allow it to pump were so blocked that the heart stopped—the precise treatment for this diagnosis is to find and open the specific blockage quickly or the patient dies. The stent rapidly inserted into the left anterior descending coronary artery by a cardiologist colleague that restored its blood flow (and the patient's life) was as true as it was beautiful to observe—it was almost poetic biology that was as scientifically precise as it was personally urgent. The treatment was a single entity (coronary stent) that could be understood as true and beautiful, the science of revascularization combined with the provider's ethical commitment to heal. As this book focuses on the single entity of the future healthcare systems' design, we do so in a way similarly that is scientific and ethical, analyzing its complementary technical AI and health equity elements. And accordingly, AI Health appears to increasingly allow us as our new paradigmatic prism to see healthcare in a new way for the future-how PrMed and PubHealth's dual contribution to

prevention, diagnoses, and treatment measures require both individual- and population-level HealthBD, with its interdependent AI analytics, to drive effective and equitable interventions (which have both individual and population aspects in addition to clinical and organizational dimensions, all within a system design model coherent unity in diversity). The practical implications of this conceptual framework include strategies, operations, investments, and wider societal collaboration within and across healthcare systems to realize this design vision as the means to the end of effective and equitable value healthcare delivery (implications which we will explore next).

3.5 Value-based system approach to precision medicine: open practically, closed conceptually

3.5.1 Open healthcare system model in AI-HealthBD

The prior chapter introducing healthcare systems did so by way of discussing the traditional definition and conceptual framework describing systems. Yet as AI and the Digital Revolution have accelerated the world's historical transition into the Fourth Industrial Revolution and its emerging global digital ecosystem, healthcare like modern society is increasingly interconnected, redefined, and opened. The neat conceptual borders for the traditional model of the system less and less map onto the practical reality of systems increasingly communicating and influencing the broader society and vice versa, opening up systems to the digital ecosystem in which they already operate (but now with increasing capacity or at least awareness to participate in the digital exchange of patients and populations "within" and "outside" healthcare systems). Contemporary healthcare systems are thus digitally open (and affected by larger societal forces) and still conceptually closed (with still prevalent ambiguous borders defining their essential constitutive parts and relationships of those parts), leaving increasing global pressure for AI-accelerated organizational and societal trends blurring the boundaries of systems by sharpening the focus on value healthcare as HealthBD increasingly unites patients, populations, and societies in ways that are increasingly actionable at the level of the patient—provider relationship and provider—administrator relationship.

Within this broader context and to bring together the trends we have explored above, digitalization's revolution reshaping contemporary PrMed within modern healthcare can be conceptualized as the integration of AI analytics of large data sources as the above AI-HealthBD paradigm oriented toward and grounded in value-based healthcare delivery (New England Journal of Medicine Catalyst, 2018). Practically, it is difficult to have AI without Big Data and vice versa. Valuable healthcare AI typically needs a lot of data, and such Big Data requires something more powerful and efficient than individual human cognitive capacities to turn digits into decisions that drive greater value healthcare delivery with greater quality and equity at lower costs. And as

outlined above, the initial phases already in this transformation demonstrate how the more sophisticated AI techniques of DL partnered with EHRs provide healthcare systems the ability to digitally unlock the data already latent in their organizational structure (through the underlying data infrastructure linking remote devices, clinics, hospitals, and other third-party entities and related stakeholders). This allows them to enhance clinically and organizationally value-based healthcare for patients and populations, through AI Health leveraging the complementary strengths and mitigating the limitations of PrMed and PubHealth.

This brings us to a more granular position to analyze the future of AI-HealthBD in PrMed, which is increasingly shaped by the "open healthcare system model." Expanding the earlier discussion of HealthBD, its sources are growing to external data sources including remote devices (including wearable devices like Apple Watches, CGMs, and smartphones), public records (including census and mortality data), payer records (including claims data), search engine data (including from Google and other marketing and technology firms), pharmaceutical and device companies (generating often large amounts of R&D data for new healthcare products and services that often include focus groups and clinical studies), government agencies, research studies, and nongovernment generic databases (including those developed as curated research and policy datasets for nonsystem healthcare stakeholders like research collaborations and nongovernment organizations including think tanks and advocacy groups) (New England Journal of Medicine Catalyst, 2018). When paired with healthcare systems' EHR, omics libraries, organizational data (spanning workforce and resource information), and financial data, the data infrastructure for HealthBD expands through internal and external data sources to mirror and overlap with the larger global data ecosystem in which systems operate more closely. This further expands the current model of healthcare systems to be "open healthcare systems" in which the traditional sharp borders of systems become more fluid and open to communicate with larger societal agents and organizations in a way that better parallels the actual reality of patients, populations, and the various influences on their health. Though these forces and data sources are already transforming healthcare systems, it is now prohibitively difficult for the majority of current systems to successfully and sustainably scale AI-HealthBD (particularly given the significant technical and regulatory barriers to data collection, sharing, storage, analytics, and reporting). Systems are already struggling to deploy AI successfully—having to do so in a way that spans agents and entities "outside" the systems is even more challenging (leaving such barriers to underscore the growing distance between average healthcare systems and such topperforming AI-HealthBD organizations like Optum, which focus on AIenabled end-to-end healthcare solutions through its payor, providers, and patients being technically and organizationally aligned toward the same shared end of optimal value-based healthcare delivery).

3.5.2 Early scaling of PrMed value use case of AI-HealthBD

Building on the AI introduction chapter, there are growing practical applications of AI-HealthBD for PrMed, which helps to reduce AI hype and clarify its actual current and foreseeable benefit (tempered by the sharpening understanding of its related remaining challenges). These use cases can be grouped into the broad categories of improved (a) prevention and diagnostics, (b) error reduction, and (c) cost control:

- (a) For prevention, the healthcare system introductory chapter already considered the use of the Apple Watch in a large pragmatic dataset to expand early detection and treatment of atrial fibrillation to help prevent its later complications (including strokes and heart attacks through appropriate anticoagulation treatment) (Perez et al., 2019). Of note, this pragmatic trial design allowed rapid, large, and real-time assessment of newly detected atrial fibrillation at the individual level by recruiting 419,297 subjects in just 8 months at fractions of the cost and time for traditional clinical trials (as no study sites and only minimal study staff were required for this study focused on user-owned remote devices which facilitated a Big Data research approach to the ML-enabled Apple Watch) (Allinson, 2021). A similar AI-guided Mayo Clinic study demonstrated that the Apple Watch could be quickly used across 2454 subjects in 11 nations to translate remote monitoring data into 125,610 electrocardiograms (ECGs) to effectively determine 81.3% of patients with heart failure with reduced ejection fraction (HFrEF), a known clinical mortality predictor especially if left undermanaged (Harmon et al., 2022). In contrast to the more traditional randomized controlled design on the same spectrum of clinical trial designs, the pragmatic approach allows real-world assessment of effectiveness of available healthcare goods and services (in contrast to the more laboratory-like constraints of explanatory randomized trials of investigational goods and services) often with much greater time, cost efficiency, and generalizability (Dal-Ré et al., 2018). AI-HealthBD helps leverage efficient analytics and large data processing to operationalize such advantages from the design innovation. These advantages are accelerated further by AI-HealthBD opening the way for a closer integration within healthcare systems of routine clinical practice and R&D pipelines including N-of-1 trials, particularly with digital health devices (as real-time AI analytics can evaluate HealthBD data streams with concurrent clinical benefit for the patient concurrently with related populations through more impactful and reliable research insights, thus allowing better design and deployment of such healthcare goods and services).
- (b) For error reduction, AI-HealthBD approaches are aggressively seeking to reduce the 7000 deaths, 7 million affected lives, and \$21 billion annually

lost in the United States alone for prescription errors (National Quality Forum, 2011). The Israeli firm, MedAware, is an emblematic example of an AI-driven personalized medication safety monitoring platform as part of this effort (MedAware, 2022). It links patients' connected devices and healthcare systems to predict, detect, and avert errors throughout the healthcare delivery pipeline, with such system supporters as Mayo Clinic, Harvard University, and Chaim Sheba Medical Center. Its ML-based platform combines AI with traditional statistics to analyze patient, institution, population, and global data sources in a curated manner (with support of clinical teams optimizing algorithm performance) to generate alerts for providers (integrated with clinicians' existing decision support systems) that boost alerts' clinical relevance by 69.0% and providers' prescription changes by 38.7% while reducing alert burden by 35.4% compared to traditional (often rules-based and less sophisticated AI or statistical-based) alert systems.

(c) For cost control, AI-HealthBD initiatives are being tested, optimized, and scaled to reduce healthcare costs principally through improved quality, safety, efficiency, and error rate. A representative example is the AI-based telemedicine platform, PreHab, which integrated smart phone data with physical therapy and an orthopedic surgery team to better prepare patients for knee replacements, resulting in significant cost reduction through decreases of 25.9% in postoperative hospital length of stay, 34.3% in home health utilization, and 20% in skilled nursing facilitation use (Chughtai et al., 2019). This personalized rehabilitation plan utilized AI to link and analyze data integrated across digital devices, telemedicine provider encounters, and hospitals to optimize patients going into surgery and so cut their postoperative costs and rehabilitation needs following surgery. Now it should be noted that designing, testing, improving, and scaling such initiatives often require significant up-front investment and specialized staff that are often out of reach for lower income systems (as introduced in the AI chapter), with often only modest to absent preliminary cost savings and often suboptimal cost-effectiveness methodology (Rossi et al., 2022; Wolff et al., 2020). A nation-wide 2020 study of healthcare system executives found that 90% believe AI will improve patients' experience, 89% report it is already improving system efficiencies, and 91% hold it is improving healthcare access, while it will have its greatest impact on diagnostics (47%), EHR management (41%), and robotic tasks (40%) though 54% assert it has increased healthcare costs (amid rising costs for design, deployment, talent recruitment and retainment, and privacy and legal risk management) (Gusher et al., 2020). As the massive costs (and initial competitive clinical and revenue advantage) for individuals and organizations developing new medical devices, products, and services historically are later diffused at significantly lower cost and barriers to use for others, AI-HealthBD costs are similarly expected to drop and adoption

increases through stronger intersystem collaboration, integration, and utilization of generic alternatives adapting the intellectual property of the above—yet their association with the related inequities which their initial design and deployment intensify is garnering increasing scrutiny and subsequent countermeasures (which we will consider in more depth in the later economic and ethics chapters). AI-HealthBD focused on reducing inequities as part of a larger strategic and tactical focus of healthcare systems is calculated in the United States alone to boost patient outcomes in parallel with a \$3 trillion annual GDP boost, generate \$4 for every \$1 invested reducing related disease burden, and save \$100 billion in costs, according to the world's largest strategy consulting firm, McKinsey and Company (Gliadkovskaya, 2022). Through more resource efficient design and deployment of AI-HealthBD, the cost savings through increased lean effectiveness for systems driven by AI-HealthBD are thus projected to more rapidly diffuse through healthcare systems (even those farther from the initial launch and scale of such interventions) increasing the more rapid and sustainable return on its investment.

3.5.3 AI-HealthBD data "oceans," value barriers, and countermeasures

Building on the prior discussion in the healthcare AI chapter on barriers to adoption, PrMed AI-HealthBD still faces significant challenges in data aggregation, policy and regulation, and management (New England Journal of Medicine Catalyst, 2018). Despite the improved insights and system decisions generating higher value healthcare with better and bigger AI-unlocked data, it is still technically difficult to access and integrate the myriad of needed datasets (in their often diverse data storage systems) and data owners (from healthcare systems to payors, technology companies, community organizations, and governments often all governed by different regulatory bodies and statutes). Moving from data "lakes" (or central repositories of raw structured and unstructured data often in cloud-based storage) to data "oceans" leverages the greater power of Big Data with the ultimate goal of translating the full global data ecosystem into HealthBD (with all the digital "streams," "rivers," lakes, and oceans) that captures and makes actionable as much of the that ecosystem as relevant to patients and populations. But even if an effective data infrastructure, interoperability, and portability design and deployment plan is created, strict and often conflicting organizational policies, association requirements, and government statutes often place prohibitively high regulatory burdens on approving and executing such plans and oversight (particularly with protected health information such as the US HIPAA [Health Insurance Portability and Accountability Act] requirements). Once data aggregation and regulatory barriers are overcome, there still remains traditional management

structures and biases that slow PrMed's AI-HealthBD utilization given the historic divide and lack of common "language" among providers, administrators, and data scientists. Regardless, the prior AI chapter and the current PrMed chapter have introduced countermeasures to respond to these challenges, including the All of Us initiative, Optum's continually growing clinical claims end-to-end dataset, healthcare AI centers for excellence, and other emerging bundled AI solutions (whose very design focuses on embedded and streamlined solutions concurrently to these technical and regulatory barriers) including the US NIH Big Data to Knowledge program, Philips's HealthSuite Digital Platform (consisting of 15 petabytes of over 390 million patient inputs, imaging studies, and medical records), and the European Union-supported European Medical Information Framework (targeting 50 million European patients' EHRs) (NIH, 2021; Wiggins, 2022; European Medical Information Framework, 2021).

3.6 Al-enabled omics in precision medicine: 60% social + 30% genes + 10% medical = health determinants

3.6.1 Mutiomics barriers and breakthroughs

Above we discussed the first pillar of contemporary and emerging PrMed, data science (focused on AI-HealthBD operationalizing a growing section of the global data ecosystem for healthcare systems' clinical and organizational decisions for patient and populations). Now we will address the other pillar-AI operationalized omics. Behavioral (including diet, exercise, and substance abuse) and socioeconomic factors (including socioeconomics) appear to drive approximately 60% of our health determinants, followed by 30% from our genes and omics and 10% by our medical history and care (McGinnis et al., 2002). And thus we have considered above how AI-HealthBD is increasingly opening up healthcare systems to data outside just the EHR to the 90% of data which determines our ultimate health outcomes (including the 60% coming from our mobile devices, IoT uses, social media interactions, and so on). IBM, the US technological company which pioneered the first practical application of AI, calculated that a single person throughout her/his lifetime is expected to produce enough health data to fill 300 million books (IBM, 2015). That is 2.33 quintillion (or 2,326,000,000,000,000,000) books across the world's 7.53 billion people globally as of 2020. The staggering and daunting volume, velocity, and variety of this HealthBD increasingly requires AI to translate it into actionable insights for healthcare systems, a need which is particularly accentuated in the scientifically complex omics field to help unlock the remaining 30% of health determinants.

Healthcare systems (particularly in the developed and increasingly in developing states) run on their EHRs as the central interface for clinical care and financial compensation (when can then have its more passive data

generation [as part of typical clinical care and billing] translated into active analysis). Pharmaceutical, healthcare device and service companies, and technology companies generate extensive R&D data. But omics data are some of the most labor-, capital-, and regulatory-intensive data sources within healthcare systems—healthcare systems have to go "out of their way" to build omics datasets typically in the form of research studies. Omics often has unclear and limited initial clinical application or return on financial investment, which thus typically restricts multiomics' primary driving agents to large government or academic consortiums in developed nations (which still face notable barriers to integrating the datasets into systems' financially compensated clinical practice once they are created). Yet combining genomics, transcriptomics, proteomics, and metabolomics into the "multiomics" datasets and data oceans (and then boosting their interoperability and portability to allow them to communicate with the larger HealthBD translated into practical decision through AI analytics) provides not only exciting promise for PrMed but also exponential challenges to their practical successes advancing valuebased PrMed (Conesa and Beck, 2019). AI and HealtlhBD challenges are similar to multiomics: data collection, storage, quality control, analysis, and practical applications, which similarly has undercut the early advancement of multiomics' contribution to PrMed. Yet unlike much of PrMed, multiomics lags significantly behind other data sources and there are currently minimal at best standards and successes thus far in sharing single omics datasets (typically only within experimental settings as part of research collaborations with narrowly focused clinical applications if they are present at all). For multiomics to realize its potential, it needs to become seamlessly integrated with data streams and oceans, synced with broader HealthBD data infrastructure, shared within and across healthcare systems and their aligned partners (from society to business to government stakeholders), clarified with well-defined and publicly supported parameters for data privacy and sharing, and operationalized with specified clinical applications within existing system's clinical and organizational workflows.

Early attempts to codify successes and define standards for multiomics support promising solutions moving PrMed applications forward. Nature, one of the world's top scientific journals by academic citation, through their affiliated journal, Scientific Data, in 2019 launched a multiomics dataset compendium spanning 6 -omics datasets: STATegra, Personal Genome Project UK, ColPortal, Potato Virus Y, Sleep Deprivation, and Fibrotic Kidney datasets (Conesa and Beck, 2019). This compendium is constituted by clinical and microbiome traits with gene, genomic, epigenomic, metabolomics, proteomics, and microRNA data from 154,723 genomes and 177 human subjects in addition to viral and mouse biological samples (including with time series data). Previously, these datasets were housed in separate public repositories based on nuances of available data technologies at the time and specific to the particular experimental objectives from their initial studies which launched

them. Such -omics datasets typically are stored according to their data or assay type (including imaging, sequencing, and assay). The Scientific Data multiomics compendium presents the first known attempt advancing the goal of a well-defined and accessible central public repository of multiomics, linked including at the individual sample level with multivariable phenotypes (allowing multiple experimental designs and diverse clinical applications). In line with the AI chapter's discussion about cloud-based technologies and innovative collaborations to leverage limited AI and Big Data capacities across stakeholders, innovative public-private partnerships including with the above compendium and the AI-supported private commercial enterprise, Lifebit, operationalize this repository through Lifebit's cloud-based hosting and integrative analysis platform with free access (Lifebit, 2022a). Further, recent advances in multiple and integrative imputation methodologies are assisting in combatting the significant challenges that missing data play in even these high-quality multiomics dataset (Voillet et al., 2016; Lin et al., 2016).

The AI-HealthBD application for PrMed was demonstrated using this integrated mutliomics' cloud-based data infrastructure with linked analytics through the 2022 launch of Lifebit's partnership with the government agency, the Danish National Genome Center (DNGC), for the Lifebit CloudOS program (Lifebit, 2022b). The Denmark public agency outsourced the need for a secure and scalable data infrastructure, management, and analysis platform to the private company, Lifebit, which in return provided a central cloud-based platform for the nation's clinicians, research, and international collaborators through the Danish national healthcare system. The Lifebit platform is linked with the DNGC's on-site supercomputing center to specifically advance the Danish healthcare system's strategic PrMed focus (which includes sequencing 60,000 patients with rare, autoimmune, and cancer diseases) while expanding its national and international AI-HealthBD infrastructure with Genomic Medicine Sweden, France Genomique, and Genomics England, among other global partners (given the exponential surge up to 100 times in scientific findings including new genomic-disease associations with each increase of just 10 times the number of human subjects including in their data sources). This real-world application extends similarly to Lifebit's partnership with the UK's government—academic collaboration of the National Institute for Health and Care Research and the University of Cambridge in their CYNAPSE clinicgenomic cloud computation platform. Lifebit similarly partnered with China's Hong Kong SAR Government through its Hong Kong's Genome Institute on the platform's application as a clinical decision support tool (particularly in rare diseases and hereditary cancers) by translating raw genomic data into clinical diagnoses in just 3 h (Garin, 2022). These government stakeholder's related healthcare systems typically characterized as more nationalized, costfocused, and state-managed or influenced (compared to the more decentralized US system) are increasingly investing in such innovative public-private partnerships in translational multiomics as part of larger AI-HealthBD

initiatives advancing applied PrMed programs for improved patient and population benefit (with improved system costs through enhanced prevention, early detection, and more effective and efficient treatments for such patients who historically are more costly healthcare utilizers through delayed diagnoses and harder-to-treat diseases).

3.6.2 Translational multiomics, pharmacogenetics, and radiogenomics use cases

These barriers and breakthroughs in AI-supported multiomics in PrMed brings us to its three overarching trends to explain leading related use cases: (a) translational multiomics, (b) pharmacogenetics, and (c) radiogenomics:

- (a) Translational multiomics: The above section has detailed the emerging use cases in PrMed of translating multiomics into actional clinical and organizational insights at the local and national healthcare system levels through omics data sources integrated with larger AI-HealthBD infrastructures, particularly through private-public partnerships (oriented toward improving local value-based PrMed and technically and organizationally linked regionally and globally to leverage such data streams and sources back into the initial above aim). A notable challenge to successful translational multiomics is social and environmental barriers to value healthcare delivery. How do you use patients' genomes to tailor their cancer treatments if they are homeless or live in resource-poor communities lacking basic and consistent access to such more sophisticated PrMed? AI is being increasingly deployed to reduce such barriers to better technically and organizationally integrate these more vulnerable patient populations to the higher resource healthcare systems, services, and products (including multiomics informed), such as with AI-powered identification of especially underreported homelessness using EHRs and DL-supported identification of infectious disease outbreaks and cervical cancer to allow more precise and efficient diagnosis and matching of system resources for these harder-to-reach and harder-to-treat individuals (Biederman et al., 2019; Chae et al., 2018; William et al., 2018).
- (b) Pharmacogenetics: Drawing on the earlier discussion about PrMed's historical development (including its early 2000s HGP-powered boost into genomics), potentially the first PrMed application at healthcare system scale was the US Vanderbilt University's genomics-assisted clinical support tool guiding the use of the clopidogrel antiplatelet drug that integrated prospective CYP2C19 gene variant mapping with an existing EHR to support providers in more tailored treatment for patients with cardiac disease (Pulley et al., 2012). This program notably included a synced clinical and organizational focus on delivering clinically effective and time-efficient recommendations for the end user (providers treating

patients) through an R&D and quality improvement pipeline that concurrently tackled such diverse challenges as institutional investment, assay reliability, usability of EHR-based point-of-care recommendations, and patient-provider engagement. This initial pharmacogenomics initiative evolved into their BioVU (DNA repository or biobank of over 278,000 samples linked to patients' deidentified EHR clinical and demographic data), including its private—academic collaboration with the AI-powered Google for AI-HealthBD R&D infrastructure, similar to the above Lifebit projects (Abul-Husn and Kenny, 2019). There is also emerging innovation pressuring such PrMed pharmacogenetics to become preemptive to identify and predict which patients will require particular genotypeinformed medications before the need arises to improve the therapeutic net benefit at lower implementation costs (Schildcrout et al., 2016). To further accelerate the successful application of PrMed pharmacogenetics, AI utilization particularly with DL is supporting how the current scientific literature can be integrated with multiomics and clinical datasets (like EHRs) to enhance prediction (particularly in gene expression, genomic regulatory elements, gene transcription initiation sites, and 3D protein configurations) and successful clinical application (accelerating the accurate and precise association of disease and genomic variation guiding effective diagnosis, prognosis, and treatment) (Zou et al., 2019). Oncological multiomics applications for AI-enabled PrMed have been particularly productive, including 34 healthcare AI uses for 14 primary malignancies including oral, colorectal, gastric, thyroid, melanoma, breast, lung, prostate, glioma, bladder, leukemia, ovarian, kidney, and liver (Patel et al., 2020). These initiatives help achieve more precise treatments for patients based on their unique tumor and clinical traits to reduce unnecessary damage from unnecessary and inappropriate treatment (such as tailoring pediatric patient's chemotherapy for medulloblastoma tumors whose exomes demonstrate they are more susceptible to chemotherapy, thus potentially saving children from the more traditional and damaging multimodal treatments of surgery and whole brain radiation which often entail negative long-term neurocognitive impacts).

(c) Radiogenomics: The AI-powered PrMed integration of gene expression and cancer imaging predicting postradiotherapy toxicity is an illustrative example of how multiomics is helping catalyze innovative and cross-discipline clinical applications by forming a more complete, accurate, and precise picture of patients and populations (Trivizakis et al., 2020). Despite data availability remaining the predominant challenge to the field's development, there have been growing successful AI-based PrMed applications identifying radiogenomic associations in colorectal, liver, breast, and glioma cancers (including noninvasively predicting glioma genotypes using MRIs) to better select optimal treatment at the individual level (Bibault et al., 2018; Trivizakis et al., 2019; Zhu et al., 2019; Chang et al., 2014).

3.7 Al-enabled data science + multiomics = Personalized medicine's future

We have explored in this chapter how personalized medicine's contemporary pillars of data science and multiomics are undergoing a fundamental revolution with the larger AI-powered digital revolution in healthcare. AI-accelerated analytics and data storage are rapidly expanding the data infrastructure of healthcare systems by opening them up to the larger global data ecosystem through more streamlined and efficient technical and organizational communication and infrastructure integration. This AI-HealthBD paradigm uniting data science (leveraging AI on population-level data to better personalize higher value healthcare for individual patients) and mutiomics (integrating the more detailed molecular data of patients with their social and environmental data) is increasingly demonstrating to healthcare systems how they can have more comprehensive, accurate, and precise understanding of populations and unique patients. And thus systems are seeing the growing successes of this emerging paradigm to improve value-based healthcare delivery not only directly (through improved prevention, diagnosis, prognosis, and treatment) but also indirectly (through AI linking this PrMed to its necessary complement of PubHealth). Thus in this chapter we have considered the emerging healthcare system model for the future: AI + healthcare Big Data (data science + multiomics) = precision medicine. This took us to the organizational synthesis of the proposed model: AI-enabled and integrated precision medicine + public health = healthcare's future. We will now pivot to investigating the PubHealth portion of this formula in the subsequent chapter as we progressively move from the slowly learning healthcare system model of today to the thinking healthcare system model of tomorrow. We will be paying particular attention to the concrete technical applications for AI, barriers to their deployment, and the health inequities worsened and improved by their applications.

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Chapter 4

AI + public health: effective and fair collaboration

4.1 History, concepts, and terms

4.1.1 Recap

Let us briefly get our bearings in this book before we move further forward together. To ultimately reach the destination of defining and describing AI's transformation of the future's healthcare system, we will need to analyze that transformation's external societal context (within the digital health ecosystem framed by and influencing patient safety and security, political economics, and ethics). And before we get to that context, we need to finish considering its internal technical context (including healthcare AI in general and AI-enabled PrMed [which the last two chapters have done], setting us up to consider AI-enabled PubHealth in this chapter). Once we finish PubHealth (including its history, trends, post-COVID pivot, and AI applications), we will consider PrMed united with PubMed as the main operational domain of the modern healthcare system delivery. And within that delivery, we will be able to consider AI-informed adaptive system design that includes structural streamlining, telemedicine, and digital engagement (including provider-patient interactions and mobile monitoring).

4.1.2 Quarantines to vaccines

Socially accepted infection control measures largely shaped the centuries of PubHealth up to the 2000s. As early as the 2nd millennium B.C., the first deliberate construction of residential water supplies, bathrooms, toilets, and drainage systems appears to have occurred in Europe (Juuti et al., 2007). The Jewish Torah as early as the 5th century B.C. Persian Empire extolled personal hygiene and diet regiments as part of larger religious practices, similar to recommendations from Buddhist and traditional Chinese medicine for well-being (and by extension disease prevention) dating back to at least the 2nd century A.D. (Chattopadhyay, 1968). Greece in the 5th century B.C. featured the first known documented attempts to provide a scientific theory of disease causation (Bryant and Rhodes, 2021). These were followed by the book, *Airs*,

Waters, and Places, attributed to Hippocrates as the first systematic formulation of a causal association between the environment and disease, paving the way for the predominant disease theory and related premodern PubHealth countermeasures for nearly 1000 years of endemics (infectious diseases in a local area) and epidemics (infectious diseases affecting a population specifically within a short time period).

In the late 1600s, European cities began naming public officials to track plague deaths and enforce quarantine measures (Goudsblom, 1986). The 19th century Industrial Revolution in Europe catalyzed the publicly recognized emergence of early modern PubHealth as a distinct scientific discipline and social enterprise (Wohl, 1983). Growing factories hungrily drove the rapid rise of dense urbanized residences with poor living conditions and sanitation, triggering recurrent waves of contagious diseases that not only caused a disproportionate burden of disease on vulnerable populations (including the poor, immigrants, and minorities) but also significant disruptions in workforce productivity (which intensified corporate pressure on governments to address such diseases). A sea change was triggered in 1838 with the British Poor Law Commission, which under the English social reformer, Edwin Chadwick (1800–1890 A.D.), produced one of the first statistical-based analyses for life expectancy across society (demonstrating a 20-year mortality disparity between the rich gentry and the poor laborer, the latter who died on average at 16 years of age) (Hanlon and Picket, 1984). Chadwick's sanitation recommendation (for civil engineering improving sewage and waste disposal) as a countermeasure for such disparities, along with numerous other recommendations from the 1838, report specifically helped produce the 1848 Public Health Act and more generally ushered in the new era of societal-scientific PubHealth (characterized by the historic integration and resultant health effectiveness of scientific analyses of disease causation and distribution, government-enforced social and civil engineering countermeasures, and social and formal education about disease prevention and treatment).

By the late 1800s, bacteriological advances accelerated PubHealth's effectiveness and social acceptance as the French chemist, Louis Pasteur (1822-95 A.D.), demonstrated in 1877 that the bacteria, Bacillus anthracis, causes the anthrax disease (Winslow, 1923). By 1884, he developed the first effective vaccine, followed shortly by European and American researchers developing vaccines for yellow fever, typhoid, diphtheria, and tuberculosis. As PubHealth entered the 20th century, it transitioned from the ancient and early modern-focused individual and societal behaviors to blunt mortality from nameless sicknesses into the later modern era of more precise, scientific, effective, and coordinated measures to target diseases (with emphasis on lower cost, population scaled interventions that better optimize well-being equitably across society). Thus in 1920, one of the seminal pioneering leaders of modern the American bacteriologist, Charles-Edward PubHealth, (1877–1957 A.D.), provided the now canonical definition of PubHealth:

The science and the art of preventing disease, prolonging life, and promoting physical health and efficiency through organized community efforts for the sanitation of the environment, the control of community infections, the education of the individual in principles of personal hygiene, the organization of medical and nursing service for the early diagnosis and preventive treatment of disease, and the development of the social machinery which will ensure to every individual in the community a standard of living adequate for the maintenance of health; organizing these benefits in such fashion as to enable every citizen to realize his birthright of health and longevity. (Winkelstein, 2022; Winslow, 1920)

By 2015, the Scottish-American economist, Angus Deaton (1945– present), was awarded the Nobel Prize in Economics, recognizing his role as one of the late 20th century's leading figures on integral human development (Bondarenko, 2021; Princeton, 2022). Highlighting the PubHealth advances of the post-20th century Industrial Revolution—immunization, antibiotics, nutrition, and sanitation—Deaton demonstrated how late modernity's concurrent and interdependent rise of health and wealth in scientific-capitalist societies produced unprecedented growth in both, along with their related inequalities (as particularly European and North American nations rapidly became healthier and richer much faster than the rest of the world as the former's PubHealth and economic innovations only later diffused to the latter). Deaton proposed how this unprecedented revolution in well-being (as the net sum of health and wealth) specifically required PubHealth programs operationalized at societal scale through sufficient political and institutional support—and that the lack of state support for such institutionalized Pub-Health investment in healthcare systems is the primary driver of societal inequalities (as the greater burden of preventable and mitigatable disease disproportionately limits poor populations from deriving equitable benefit from economic growth). Poor education implicates poor diffusion of technological innovation across societies which in turn perpetuates the cycle of poverty, sickness, poor economic productivity, and thus reinforcing intergenerational poor education for these socially disadvantaged groups (making their children more likely to face greater difficulty escaping from this cycle). The lack of sufficient well-being-orientated PubHealth capacities and networking among government, business, academic, and community organizations thus manifests the inadequacies of synergistic institutionalized well-being. The 20th century therefore culminated in a more integral vision of PubHealth as fundamentally important (if not necessary) for sustained and equitable societal, political, and economic stability and growth. The rich and healthy cannot remain rich and healthy for long without sufficient PubHealth investment to empower the poor and sick to become less so, according to Deaton. Such a PubHealth conception of integral development (linking health and political economics) emphasizes how sustained efficiency growth requires sustained equity improvement.

4.2 "Global health" reformulation and anticolonial resistance

4.2.1 PubHealth's conceptual reformulation as "global health"

In the century following 1900, PubHealth advances including in vaccination, sanitation, noncommunicable disease prevention, workplace safety, mother and child health optimization, and diet improvement produced 25 out of the 30 years of improved life expectancy (nearly doubling life expectancy) (Groseclose, 1999). Crossing the threshold of the 2000s, the global PubHealth consensus largely was one of optimism in the envisioned continued linear population-wide health improvements as PubHealth exploded (principally as international, state, and local government and community organization-driven programs continued this steady march of progress, alongside medicine which developed largely during this same time in modern healthcare systems). This hope was emblematically articulated in 2013 by the Lancet Commission on Investing in Health (CIH) with its global health investment framework, the Global Health 2035 (Jamison et al., 2013). This commission was driven by Lancet, one of the oldest, most prestigious, and most cited peer-reviewed medical journals on the planet, affording CIH a stable international audience and support base from the medical and PubHealth communities (Jemielniak et al., 2019; Lancet, 2022). The Commission argued that by leveraging Pub-Health's growing technical and financial capacities for sufficient "health technologies and systems" (particularly in reducing noncommunicable diseases and improving universal health coverage), a "grand convergence' in health would be achievable within our lifetimes" by slashing infectious, child, and maternal mortality rates in low- and middle-income nations so they could approach the best-performing middle- to high-income nations by 2035, saving 10 million lives during this time, and producing financial benefits minus costs by up to 20-fold.

The 2010s saw a more fine-tuned redesign and reformulation of PubHealth as "global health" with a growing push across government, academic, and community organizations to internationally adapt Wislow's definition of PubHealth (Fried et al., 2010). The growing technical effectiveness of Pub-Health interventions to improve population-wide health outcomes and the concurrent growing societal support for such measures increasingly translated into conglomerated stakeholders focusing on more equitably distributing those benefits with a growing multidisciplinary integration of clinical, populationwide health, sociocultural, political economic, and environmental factors. The Consortium of Universities for Global Health (CUGH), founded in 2008 by the US Bill and Melinda Gates Foundation and expanded to 170 institutions worldwide by 2022, defined global health as "a field of study, research and practice that places a priority on achieving equity in health for all people" (Koplan et al., 2009). CUGH, as a leading influential global health voice,

'broadened' the mission of PubHealth "to improve the wellbeing of people and the planet through education, research, service, and advocacy" (CUGH, 2022).

The formal international definition and operationalization occurred through the 2006 Health in All program (by the WHO-hosted European Observatory on Health Systems and Policies) and the 2007 multinational sponsored Oslo Ministerial Declaration (supervised by the Ministers of Foreign Affairs of Brazil, France, Indonesia, Norway, Senegal, South Africa, and Thailand) (Ståhl et al., 2006; Ministers, 2007). The culmination of PubHealth as global health's expansion into (and even in part coopting) political economics was cemented by the 2008 UN General Assembly adoption of the resolution, "Global health and foreign policy" (UN, 2009, 2008). It urged nations to recognize "their interdependence" under the unified conceptual framework of "global public health," and so "consider health issues in the formulation of foreign policy" for "achieving the health-related Millennium Development Goals," advanced by its 2009 council report. It took over 2000 years for PubHealth to develop from socio-cultural practices to political economic programs to the scientific discipline of "public health." And it took 20 years for PubHealth to expand to a foreign policy and international institutional structure of "global health" for the ultimate stated goal of equity for all individuals and populations.

4.2.2 Anticolonial critique of global health

But despite this prominent pivot in PubHealth, there has been sustained criticism that the absence of strategic, methodological, or even geographic distinctions between PubHealth and "global health" means that at most global health is "public health somewhere else," as stakeholders "practice public health" in a community or political entity separate from the ones they identify as their home (King and Koski, 2020). Such criticism even more fundamentally questions if global health has embedded "inherent colonialism, uncritical faith in Western expertise and technology, [and a] lack of accountability and inefficient use of resources" (Packard, 2016; Horton, 2013; Deaton, 2013). Following the French philosopher, Jean-Paul Sartre (1905-80 A.D.), who coined the term "neo-colonialism," there were deepening parallel concerns about such global health being part of a larger late modern economic or cultural reimposition or continuation of imperialist rule by a stronger (often former colonial) state over a weaker (Sartre, 1956; Stanard, 2018, p. 5). In place of for instance the military control of European colonial powers in the 1600-1900s throughout Africa, the Middle East, Asia, and the Americas, subjugation of weaker states by neo-colonial powers in the late 1900s and early 2000s was manifested as economic and often intertwined cultural imperialist forces that produced or accelerated often political economic dependence of weaker states on the stronger, often in the form of political manipulation and unstainable debt obligations born by weaker states in

contrast to their own self-identified values and preferred cultural, political economic, and societal arrangements (Prashad, 2007, pp. 231–233). Similar to the widespread resistance in low- and middle-income nations against so-called neo-colonialism that strengthened during the 2000-10s against Western-led international aid and China-led infrastructure investments (Chatzky and McBride, 2020), such critique even from within the aid and investment stakeholder community has been articulated by Angus Deaton as the following:

Why is it we who have to do something? Who put us in charge? We often have such a poor understanding of what they need or want, of how their societies work, that our clumsy attempts to help on our terms do more harm than good ... And when we fail, we continue on because our interests are now at stake—it is our aid industry, staffed largely by our professionals, and generating kudos and votes for our politicians—and because, after all, we must do something. (Deaton, 2013)

Deaton's research suggests that such dominant international aid including within larger PubMed programs is generally ineffective at best and counterproductive at worst, as sustained integral development particularly through PubHealth requires a more organic and subsidiarity-focused approach (including through capacity-building approaches i.e., enhanced education and institutionalized investment to help nations realize their self-identified development objectives, respective of their shared values). The African-born philosopher and first Prime Minister of Ghana, Kwame Nkrumah (1909–72 A.D.), took this critique further to assert that PubHealth interventions as "Health Clinics and Housing" (as advocated in the April 1965 Bulletin produced by the US-based and UN-neighbored American Federation of Labor and Congress of Industrial Organizations [AFL-CIO] was explicitly meant to create African unions dependent on American unions) are integrated within and advance larger neo-colonial drivers including to ultimately "expand American capital investment in the African nations," leaving the latter and other neo-colonized states to have the illusion of "international sovereignty" but "[i]n reality its economic system and thus its political policy is directed from outside" (Nkrumah, 1965, ch. 18, 1).

The Harvard University and Rwanda-based University of Global Health Equity physician-anthropologist, Eugene Richardson, pushed further to argue in a Foucoult-like approach that even PubHealth's methodologies (including epidemiological modeling, infectious disease containment, AI and Big Data, and causal inference statistics) actually "play an essential role in perpetuating a range of global inequities" (Richardson, 2020, Summary; Foucault, 1984). Accordingly, the central PubHealth tool of disease causation models "serve protected affluence" by "setting epistemic limits" (or what can be known) on accounts of sick versus healthy groups, feeding the "biggest epidemic" the

world faces, namely, "an epidemic of illusions" that is "propagated by the coloniality of knowledge production" to "achieve monopolies on truth" (p. 5).

Yet this critical position largely remained throughout the 2010s the minority position, questioning the expansion of PubHealth outside the "boundaries" of more localized and regional healthcare systems and healthcare policy to the international realm with questionable motives at worst and questionable outcomes at best, leaving largely intact PubHealth's growing societal influence and investment within and outside healthcare systems. But this linear surge forward (to invoke the previous PrMed chapter's discussion about Chaos Theory) appeared to be able to continue indefinitely—until it slammed into COVID-19.

4.3 The great COVID reset

4.3.1 From COVID-19 stress test for PubHealth to AI pressure for PubHealth redesign

By 2020, there was a growing consensus of prominent critics globally that COVID-19 fundamentally challenged the road on which modern PubHealth was traveling, forcing a worldwide reckoning of fundamental deficiencies not only in healthcare systems but also the larger sociocultural and political economic systems-but COVID's Great Reset gave the modern world and modern PubHealth a chance to pick a potentially better road into a better future (Schwab and Malleret, 2020). Despite the unprecedented advanced health, science, technology, political economic, finance, and communication systems in the 21st century which modern PubHealth drew on, COVID-19 became one of the top 10 most deadly pandemics in history, without any clear consensus that PubHealth's government and societal collaborative interventions had sustained net benefit reducing such poor outcomes, especially their disproportionate burden on low-income communities and nations (according to the CDC, WHO, John Hopkins University, and Encyclopedia Britannica data) (LePan and Schell, 2020; Varma, 2022). Such influential voices even within modern PubHealth have gone so far as to assert that COVID did not simply reveal weaknesses and even failures in modern PubHealth, but that "public health [itself] failed" (Varma, 2022). Contemporary PubHealth has the most sophisticated scientific and societal tools it has ever wielded (including a global digital ecosystem linking the world's peoples and the most advanced healthcare systems in history)—and yet there is no clear international agreement what if any of the PubHealth measures had sufficient benefit surpassing their costs (as the limits of collective action became starkly more apparent as the pandemic dragged on). What went wrong?

On December 31, 2019, China reported a cluster of novel pneumonia cases in its Wuhan Hubei Province, then by January 13th of 2020, the first case outside of China was detected in Thailand, and by March 11th the WHO declared it a pandemic (WHO, 2020a). By December 31, 2020, the global deaths had topped 18.2 million (95% uncertainty interval 17.1-19.6) with excess mortality of 120.3 deaths per 100,000 people (with the highest rates in India, Russia, Mexico, Brazil, Indonesia, and Pakistan) (Wang et al., 2022). By January 2022, the International Monetary Fund (IMF) calculated that COVID-19 over its first 4 years is expected to drain \$12.5 trillion from the global economy, or nearly 1 of its every 10 dollars (IMF, 2022; Hamadeh et al., 2020). In the healthcare system chapter, we already analyzed how vaccine nationalism may cost upwards of \$9.2 trillion total of that cost (Cakmaklı et al., 2021), while rich nations received 84% of the first year of all COVID-19 vaccines compared to 1.1% of low-income nations. We already considered the urgent critique of Dr. John Nkengasong, the Africa CDC Director, that such vaccine inequity—which seemingly defies not just globally shared ethical norms but also undermines health and economic costs (including for highincome nations)—as a "collapse of global cooperation and solidarity" (Myers, 2022).

After 2 centuries of the scientific revolution in modern PubHealth which matured into its international institutionalized cooperation of the first 2 decades of the 21st century, it appears increasingly that COVID-19 represents an unprecedented modern stress test for PubHealth, with ongoing debate globally whether it was an unqualified success or failure (Ghebreyesus et al., 2022). Despite PubHealth's major successes up to 2019, major critics have asserted that the pandemic exposed persistent "long-standing systemic inequalities in the US health care system result in the tragically unequal effect of COVID-19" which are only more prominent internationally, demonstrating that states across the globe are "failing another ... stress test on health disparities" (Owen et al., 2020). With the vast majority of the health and financial burden from COVID-19 borne by lower-income individuals, communities, and nations, it was reportedly clear according to a Harvard analysis (published in the peerreviewed scientific journal, Global Public Health) even in the first 2 months of the pandemic that COVID illustrated the urgent necessity to "reimagine and repair the broken systems of global health," as it laid bare the "hollowness of the global health rhetoric of equity, the weaknesses of a health security-driven global health agenda, and the negative health impacts of power differentials not only globally, but also regionally and locally" (Shamasunder et al., 2020).

If there has been rampant and sustained critique even among the current thought leaders of PubHealth asserting its shortcomings for COVID-19 (along with questioning the efficacy and even validity of its traditional structures, norms, assumptions, and methodologies), then does this suggest AI may help plug the gaps and accelerate a more effective and equitable digital revolution in PubHealth? (like how we explored its concurrent impact in PrMed). Can AI make PubHealth more precise, local, and fair, empowering local communities with the tools to care for their own communities (in collaborative solidarity and balanced interdependent relationships)? A classic adage about the

distinction between medicine and public health is that the former is like bailing water in a flooding room, while the latter is like turning off the faucet. Can AI help us do both well (to help us not fail the next local or global stress test?). Does the Great COVID Reset in PubHealth, constituting wide intersector societal support internationally for not just improved but new approaches to next-generation PubHealth, thus require not only new (noncolonial) frameworks but also new (AI) methodologies?

4.3.2 Post-COVID ethical AI reset for PubHealth

Accelerated by the pressures, failures, and lessons of COVID-19 particularly in the breakdown of effective PubHealth responses, a mounting mass of organizations have turned to "ethical AI" amid global digitalization to catalyze equitably effective and coordinated PubHealth solutions, both locally (through healthcare systems) and internationally (through complementary healthcare policies and programs)—respecting individual, population, and state sovereignty amid pragmatic recognition of differing values, capacities, needs, and interdependencies across the above groups. Similar to growing efforts to "practice public health" by recovering a more societally supported PubHealth model with support of patients and populations freed from "neo-colonial restraints," AI-enabled PubHealth similarly has undergone increased scrutiny fundamentally (principally, how to make it "ethical"). The February 2020 Rome Call for AI Ethics—coordinated by the Catholic Church's Vatican City and cosigned by Microsoft, IBM, the UN Food and Agriculture Organization (FAO), and the EU's Italian Ministry of Innovation—created the first global standard and interdisciplinary pledge for coordinated AI ethics (FAO, 2020; Vatican, 2020). The above collaboration focused concurrently on practical coordination and educational theory, awarding during the same ceremony the world's top doctoral dissertation on AI ethics to a pluralistic global bioethics framework, the Personalist Social Contact (Monlezun et al., 2020, p. 35; Garcia, 2020; Monlezun, 2022). This framework unites PrMed and PubHealth along with the world's diverse belief systems through a convergent consensus model respecting the complementary sovereignty and scope of each of the above—which we will explore more in the AI healthcare ethics chapter.

Though the Rome Call received criticism similar to prior UN and global PubHealth resolutions for being excessively impractical, ambiguous, and devoid of sufficient enforcement mechanisms, its central principles (responsibility, transparency, impartiality, inclusion, reliability, and security/ privacy) articulated a growing common conception of ethical AI-based approaches for cross-sector collaboration of governments, nongovernment, and corporations, ultimately underpinning efforts to advance next-generation PubHealth (Kahn, 2020). Subsequently, the EU and US Department of Defense (DoD) both released their ethical AI guidelines and strategies that same month reflecting notable overlapping consensus on the Rome

principles (EU, 2020; DoD, 2020). The WHO followed this growing trend of Rome's principles for ethical AI (specifically for PubHealth operating through and alongside healthcare systems) with their June 2021 report, echoed by UNESCO similarly in their November 2021 report (additionally emphasizing the principles' translation into national legal frameworks) (WHO, 2021a; UNESCO, 2021).

4.4 Emerging trends framing ethical Al-enabled PubHealth

The above societal resistance to the supposed neo-colonial-like conceptual reframing of PubHealth (as "global health" in the 2000-10s) and its COVID-19 operational failures (during the critical first 2 years of the pandemic to equitably coordinate effective countermeasures especially vaccines) therefore have led to a concerted conceptual and technical refinement of ethical AI-enabled PubHealth (within the larger AI-HealthBD trend the last chapter on PrMed first introduced). Before we get to practical applications of AI-PubHealth in general and its increasing integration with healthcare systems, we will first analyze the major societal trends framing those applications: (a) digitalization, (b) demographics, and (c) deglobalization.

(a) Digitalization: COVID-19 accelerated the urgency and investment in digital cooperation for and reach of PubHealth globally. The July 2019 report, "The age of digital interdependence," by the UN High-level Panel on Digital Cooperation (chaired by Chinese businessman, Jack Ma, and American philanthropist-computer scientist, Melinda Gates) published the following recommendations to optimize the value of digital technologies as means of attaining the health-focused Sustainable Development Goals: develop an "inclusive digital economy and society" that accelerates "human and institutional capacity," by defending "human rights and human agency" through "global digital cooperation" (across governments, businesses, academics, and communities) which advances "digital trust, security and stability" (UN, 2020). The 2020 UN recommendations, meant to catalyze the urgent implementation of these strategies amidst the pandemic, were adapted by the WHO for eight principles for the "digital transformation of public health": universal connectivity, digital goods, inclusive digital health, interoperability, human rights, AI, information security, and PubHealth architecture (Garcia Saiso and D'Agostino, 2021). Coined as "artificial intelligence for public health" or AI4PH, the WHO specifically calls for its related "participation in global cooperation" with "secure, reliable, and open algorithms" through "multisectoral and interdisciplinary networks" as "part of Public Health policies," by "understanding the individual and social dimension in a globalized and interconnected [digital] reality that belongs to the human condition" (p. 5). These strategies focus on increasing peoples' safe, reliable, and private

access to the global digital ecosystem through the internet and AI-enabled related products and services as basic public digital goods, making the ecosystem more inclusive and effective as means to enhance health, and thus respecting individuals' rights for such goods to advance their individual and societal flourishing. The WHO's 2021 "Global Strategy on Digital Health" subsequently provided an overarching framework for guiding principles, strategic objectives, and an actionable implementation plan to ultimately "strengthen health systems through the application of digital health technologies for consumers, health professionals, health care providers and industry toward empowering patients and achieving the vision of health for all" (WHO, 2021b). The WHO specifically recommended AI-enabled PubHealth as "artificial intelligence solutions and big data analyses" to "improve the quality of health care and research effectiveness," with focused implementation objectives on their related "sustainable financing models," "sharing of learning," "principles for ... [their] ethical use," and appropriate "governance structures" (pp. 12, 15, 23-24). But despite such international strategic collaborative efforts, the academic community has not settled on a consensus even for the definition of "digital public health" amid the growing support for "digitalization" (integrating PubHealth operations with digital technologies) and "digital transformation" (as the cultural shift reconfiguring PubHealth services according to digitalization helping better identify and address PubHealth needs) (Iyamu et al., 2021).

(b) Deglobalization: The 2008 Great Recession, 2016 Brexit referendum and U.S. President Donald Trump's election, the 2020-21 COVID-19 initial pandemic phases, and the February 2022 Russian invasion of Ukraine quickened the late modern era of (postpeak globalization, or late modern) deglobalization, with profound influences on PubHealth (Irwin, 2020). This deglobalization refers to the process of reducing global economic interdependent integration typically in favor of protectionism (emphasizing domestic industries while resisting foreign actors). The last deglobalization phase was the 1914-45 period between WWI and WWII, leaving the 1945-2008 period as the longest and biggest surge in U.S.style liberalism-driven globalization (as measured by the sum of world imports and exports divided by global GDP), coinciding with the longest and biggest surge in PubHealth's technical effectiveness and societal influence. In a simplistic explanation, wealth and health were the tools utilized to advance the democratic global political reach of the US and its WWII allies as PubHealth became increasingly intertwined with growing global supply chains. This trend rose with China's later 2010s inward turn along with President Trump's "America First" policy and surged with COVID-19 as lockdowns unequally struck nations differently, reinforcing growing public pressure for greater domestic dependence (and reduced cross-border free flows of data, trade, capital, technology, ideas, and

people [students, tourists, and workers]). It should be noted that the post-2008 "slowbalization" term is gaining traction as the more accurate description of this current phase (as a hybrid of globalization and deglobalization) in which global trade grows but at a slower pace from the late 20th century globalization (up to the 2008 Recession) with shortened supply chains through a more refined and restricted set of trade partners, often those sharing similar sociocultural and political-economic values (i.e., with the West's liberal democratic capitalism compared to the East's more autocratic capitalism or capitalist socialism) (Lemco et al., 2021, p. 8). The U.S President Joe Biden and the federal administrative branch of government continued Trump's domestic focus by at least partially using PubHealth to justify this more deglobalization-like pivot (Sullivan and Deese, 2021). His White House report, coordinated with the Departments of HHS and DoD, advocated for more "resilient supply chains" through "friend-shoring" (focusing supply chains with nations sufficiently sharing similar values and principles), since reportedly the "COVID-19 pandemic highlighted the critical importance of a resilient U.S. public health industrial base" guided by an enhanced "supply chain resilience strategy" as part of the "six critical industrial base sectors that underpin America's economic and national security" (pp. 4, 8–9). So when nations' economic stability and national security concerns consume or co-opt PubHealth, how does "global public health" function? Practically how can future pandemics be prevented and mitigated when the AI-enabled shared digital ecosystem leveraged by PubHealth is structurally sectioned off into nations who decline to share the needed data, technology, and personnel? Additionally, rising geopolitical tensions between the Global West (the United States, Europe, Japan, Australia, and their allies) and the Global East (China, Russia, and its allies including Iran) seeking increasing influence on the largely nonaligned Global South (particularly South and Central America and Africa) have sharpened the at least rhetorical defense of human security as a fundamental PubHealth good. This security refers to the individual "freedom from fear and want" to ultimately "protect the vital core [wellbeing] of all human lives in ways that enhance human freedoms and human fulfilment" to pursue self-identified goals, unhampered by "ill health" and the threats of wars, disasters, pandemics, and socioeconomic stressors (Takemi et al., 2008; Anand, 2012). The most severe and widescale human security threat to PubHealth as of early 2022 is the Russian invasion of Ukraine (and the West's resultant socio-cultural and political economic attempts to isolate Russia from the international community and quicken the war's end), pressuring the healthcare systems of the latter into war-time transformation of its PubHealth structure and operations: community hospitals were retooled as field hospitals, rapid transfers of providers and patients were completed as the WHO documented frequent Russian targeting of healthcare facilities, Ukraine's

Alliance for Public Health delivered 140 metric tons of medical supplies to hospitals (between March 23-April 6th alone) along with nation-wide distribution of HIV/AIDS (human immunodeficiency virus/acquired immunodeficiency syndrome) antiretroviral and antituberculosis medications, mobile clinics transformed into frontline humanitarian aid distribution centers, healthcare volunteers utilized Facebook and WhatsApp digital platforms to coordinate matching of population needs with available resource distribution, and WHO supported disease surveillance and humanitarian health delivery (Simoneau and Khan, 2022). Ukraine appears to increasingly serve as one of the most informative models for PubHealth resilience in an increasingly deglobalized or at least more segmented slobalized world. As nations face increased pressure to either invest in PubHealth or defense, there is projected to be increased geopolitical stressors for PubHealth to complementarily (without being coopted) collaborate through healthcare systems with political economic structures to optimize human security (including its health, political, and economic dimensions).

(c) Demographics: Sustained below-replacement fertility rates particularly in developed nations (notably in East Asia, North America, and Europe) and increased life expectancy produce an unprecedented challenge for human history: how do you govern a nation or provide healthcare when there are less and less rich and working citizens and more and more poor and retired citizens (Weng, 2010). By the 2060s, such trends are broadly expected to create new or accelerating already underway population implosions in multiple nations (such as Japan and China losing up to half their population by then), triggering increasing international political economic instability as supply chains are further disrupted with the bulk of global population shifting to the Global South notably Africa. Altogether, depopulation and deglobalization pressures (limiting immigration) are expected to shrink the global population after 2064 with 183 of 195 nations persisting below replacement rates, leading to expected increased geopolitical conflict and instability as political economic centers shift to the South—likely taking PubHealth's primary stakeholders and players with it (Vollset et al., 2020) China is the prime example of these demographic trends as it manifests one of humanity's fastest economic and health rises by GDP and life expectancy respectively throughout the 1990-2000s (with significant mortality reduction through PubHealth investments reducing communicable and poverty-related diseases), and then by the 2020s becoming one of the fastest aging populations—or the first modern nation to grow old before rich (CSIS, 2020; WHO, 2022). Meanwhile, notwithstanding the vibrant state and local-level diversity, Africa lags the rest of the world's regions in life expectancy and health improvements (particularly sub-Sahara) (Kuate Defo, 2014). Despite significant PubHealth-related mortality reductions (particularly related to

children and HIV/AIDS), persistent poverty, epidemics, and wars continue to inflict heavy African population burdens of disease relative to the rest of the world (along with continued PubHealth underinvestment and performance). The more advanced PubHealth programmatic and data infrastructures in developed nations will accordingly face increased difficulty sustaining the management and financing of these structures, as the emerging South societies will face increased pressure to scale up their own PubHealth infrastructure with the world's demographic and political economic momentum shifting to them.

4.5 Al-enabled PubHealth piloted applications

Within the context of these trends, there are a growing number of AI-enabled PubHealth piloted applications which we will survey below, followed by considering how healthcare systems are seeking to institutionalize them. Accelerated by the COVID-19-related explosion of public-private support and financing, AI-augmented PubHealth applications have significantly expanded since 2020 (Monlezun et al., 2022a). These applications can be categorized according to (a) population health, (b) precision PubHealth, and (c) system optimization:

(a) Population health: As clarified by the American Public Health Association's American Journal of Public Health and the New England Journal of Medicine (NEJM), "public health is about what we're doing as a society and population health [PopHealth] is about what a system is doing for their community" (Bharel and Mohta, 2020; Roux, 2016). The CDC specifies that PopHealth "an opportunity for health care systems, agencies, and organizations to work together in order to improve the health outcomes of the communities they serve," while the U.S. National Academy of Medicine emphasizes that PubHealth is "what we as a society do [collectively] to assure the conditions in which people can be healthy" (IoM, 2002). PopHealth thus is generally seen as the PubHealth that is within the clinical medicine-driven healthcare systems. It reaches outwards to address patients' health outcomes and their related equity (using much of the similar concepts, methodologies, and programs that Pub-Health does, yet the latter does so more through government and community organization-driven interventions in parallel with healthcare systems rather than originating within them). Additionally PubHealth largely assumes and widely invokes the "principle of social justice" as the fundamental justification for and appeal to a common moral standard for its interventions, while PopHealth has more traditionally been driven for improving health outcomes for its patients aggregated into larger populations (through intersector collaboration and broader vision of nonmedical drivers of health) and the related costs (including for the

systems caring for those patients) (Jha, 2019; Bharel and Mohta, 2020; Kelley et al., 2020). As such, AI is particularly well positioned to enhance PopHealth interventions with its emphasis on large and complex data and relationships of factors impacting health outcomes.

- i. Pandemic prevention: The AI-based private Canadian "biothreat intelligence platform," BlueDot, generated in December 2019 the first known alert for a cluster of Chinese flu-like pneumonia cases which could become a pandemic, and then produced the first scientific publication on the later named COVID-19 by accurately projecting its initial international spread that would enable its transition into a pandemic (Bogoch, 2020). BlueDot features an AI-driven integration of real-time scientific, travel, government, and traditional and social media to identify possible emerging infectious disease threats which are subsequently curated by its PubHealth professionals (including epidemiologists) along with physicians and data scientists to confirm threats and alert their clients accordingly (typically governments and corporations), thus making at least theoretically possible early, proactive, and potentially decisive countermeasures to even prevent pandemics. Early detection of pandemic-level threats when paired with effective and reliable early vaccine creation and deployment (which we will explore below) may effectively keep emerging infectious disease clusters to just that rather than progressing to pandemics (and even to endemics—though significantly more research is required to confirm this). ML has additionally been used to precisely model how and how quickly the pandemic could develop to enable more effective PubHealth responses globally (including helping healthcare systems better resource the likely harder hit areas before surges reach those regions) (Tuli et al., 2020).
- ii. COVID-19 vaccine: A 2022 meta-analysis of 18,590 studies led by John Hopkins University's Steve Hanke (a global thought leader on economic development) concluded that society-wide COVID-19 lockdowns reduced mortality only by 0.2% (with similarly little to no reduction for shelter-in-place and business, school, and border closure policies), though they had far greater even "devastating effects" worsening economic and larger PubHealth outcomes (including economic insecurity, poverty, starvation, unemployment, education deficits, domestic and civil violence, and political unrest-related morbidity and mortality) (Herby et al., 2022, p. 43). After the pandemic's first year, the WHO highlighted the disparity dimension of lockdowns (or large scale often society-wide movement restriction and physical distancing policies usually made mandatory through government enforcement) which can have "profound negative impact," disproportionately born by poor and migrant populations, and so more "targeted interventions" are preferred (WHO, 2020b).

(b) Precision PubHealth: The US CDC and NIH note how the precision approach (right treatment at the right time for the right patient) of PrMed is increasingly being broadened to whole populations in the parallel field of "precision public health" (Khoury et al., 2018). As the early 21st

century witnessed how AI-HealthBD has been transforming clinical medicine into PrMed, it has similarly introduced a similar specialization within PubHealth (Arnold, 2022). Precision PubHealth integrates not only genomics and multiomics (like PrMed) but also the more traditional PubHealth focus areas of sociodemographic, geographic, and environmental factors including PopHealth's focus on biomedical data at a population level (with AI-HealthBD helping make this conceptual development an operational reality by generating sufficient data and reliable analytics to augment practical clinician and healthcare system decision making).

- i. Real-time modelling-based decisions: Precision PubHealth has accelerated the speed, scale, and success of modern PubHealth to do what one of its primary founders first set out to do-tailor health policies as precisely as possible for maximum and equitable societal benefit. The British physician, John Snow (1813-58 A.D.), went door to door to slowly trace a cholera outbreak to the Broad Street public water pump. A contemporary larger version is the "hyper-local public health" open-source data-analytics program named SaTScan (Arnold, 2022). This 2020 digital mapping provides near-real-time high spatiotemporal resolution of COVID-19 clusters (integrating hospital, laboratory, census data, and social network data) to enable more precisely distributed protective equipment and testing and so more efficiently allocate limited healthcare system resources. A related example uses ML to screen EHRs to accurately identify patients with undiagnosed familial hypercholesterolemia to avoid wasted resources from unnecessary broad testing for what can be a rapidly lethal disease at a young age. When ML is applied to imaging scans, it can help to identify patients at increased genetic risk of developing cancer even if they are traditionally in the lower-risk group of those without a family history of cancer.
- ii. AI analytics: ML application is lagging behind the analytic demand of precision PubHealth, particularly as it relates to AI causal inference (allowing various healthcare policy and system programs to be simulated, tested, and scaled as safely and efficiently as possible) (Flaxman and Vos, 2018). ML appears to outperform standard statistical regression techniques in targeted maximum likelihood estimation to provide doubly robust estimates of average treatment effects of interventions in observation studies (in contrast to traditional alternative techniques of propensity score or inverse probability weighting) (Schuler and Rose, 2017). Unlike in randomized clinical trials where drug A is tested compared to drug B (and any difference in outcomes is typically attributed to differences in treatment not any other factors), demonstrating causality for PubHealth interventions is generally impractical, implausible, and even unethical (how do you

randomize population A to clean water supplies and population B to dirty water supplies)? Consider if such ML-enabled causal inference methodologies for precision PubHealth could have been deployed in January of 2020 to determine if governments and healthcare systems should prioritize the PubHealth intervention of lockdowns vs. early vs. delayed vaccines after considering the genome to genomic-clinical interaction between COVID-19 and humans?

- (c) System optimization: Extensive research strongly suggests that the persistent ineffectiveness and inequity of contemporary PubHealth efforts follow from their fundamental weaknesses in the design of healthcare systems, as such efforts typically prioritize disease-specific programs (set particularly by the West's American and European-led, principally funded, and overrepresented institutions including the NIH, Welcome Trust, and the World Bank) without any sustained or substantive capacity building or overall performance improvement in systems (Birn, 2014). Coupled with the "brain drain" (of medical providers and researchers being drawn to the Global North from the South) and neo-colonial undertones of "human security" paradigms in PubHealth (focusing resources on such diseases as pandemics that threaten wealthier nations while deemphasizing the larger burden of chronic diseases plaguing poorer nations), the current top-down North-dominated design deficits for PubHealth systems and those networked with healthcare systems manifest in perpetuation of such ineffectiveness and inequities. But PubHealth AI applications appear to be re-empowering systems locally to define and improve their own systems themselves.
 - i. Intervention design: ML is increasingly used to optimize more local, end-to-end, full-network disease modeling in which improved causal understanding of factors of disease development, interventions, and outcomes allow improved design, simulated deployment, actual deployment, and rapid revision of more precise PubHealth interventions (Mhasawade, 2021). ML allows more complex causal inference-informed system dynamics modeling of socio-ecologically framed individual and group-based interventions (broadly viewing health as social, mental, and physical wellbeing of societies [as communities of individuals in relationship with each other]) including in pandemic resource distribution, nutrition, smoking cessation, geographic-dense diseases, depression management, mobile-data augmentation, ACO initiatives, and even tax codes.
 - ii. Inclusive international governance structures: The worldwide shift in demographics and societal acceptance of greater inclusivity strengthens the growing healthcare systems-based PubHealth AI applications accelerating (and being accelerated by) more balanced representation and governance in international PubHealth organizations. The majority of HealthBD and healthcare AI algorithms and

applications are developed in higher-income nations and systems which thus undermine their effectiveness and equity when applied in lower-income regions, a challenge receiving increased attention particularly in Africa (Owoyemi et al., 2020). After the Ethiopian PubHealth researcher, Dr. Tedros Adhanom Ghebreyesus (1965—present), in 2017 became the first African to lead the world's leading PubHealth agency as its Director-General, the WHO has sought to address this dual deficit internationally including through fundamental and operational readiness in AI (Ghebreyesus and Swaminathan, 2021).

- 1. Fundamental readiness: The WHO's efforts in fundamental readiness relate to the technical and organizational structures and capacities to enable healthcare AI applications, particularly in data infrastructure, high-quality universal internet access (eventually for telemedicine), and ultimately for "intelligent connec tivity" (with AI-driven IoT and 5G linking particularly lowerincome nations and healthcare systems with the larger global digital ecosystem to securely share data and mutually benefit from the higher order AI algorithms and applications which inform them). Dr. Tedros led the UN's private-public Broadband Commission for Digital Development which built and distributed a repository for resilient connectivity to share the intellectual property with lower resource communities toward this fundamental readiness, as the WHO's Department of Digital Health actively collaborates with states to accelerate their healthcare system's adoption of digital health infrastructures both internally and externally (linked to the global digital ecosystem). Mutually beneficial PubHealth AI systems are an extension of this intelligent connectivity as the WHO Hub for Pandemic and Epidemic Intelligence (similar to BlueDot but with publicly accessible results) launched in 2021 to share not only data among lower and higher-income nations but also early warnings through the use of super-computing to predict emerging pandemic-level threats and inform earlier and more precise local and globally coordinated PubHealth interventions (UN, 2021).
- 2. Operational readiness: This readiness refers to the capacities for sustainable and responsible healthcare AI applications with a focus on sufficiently trained workforces and trustworthy governance structures. Similar to the 16th—19th century's European and American colonial powers extracting raw material resources and cheap labor for the political economic profit of their states (and the subservient impoverishment of the colonized poorer states), there is ongoing risk of healthcare AI applications and PubHealth interventions principally created in the Global North

and deployed in the Global South (imposing agendas on poorer communities and data extraction from them to inform these international algorithms). The 2021 collaboration of Dr. Tedro's WHO and the G7 featured efforts to advance internationally accepted ethical and regulatory standards for healthcare AI governance from a top-down approach (developed transparently and cooperatively with higher- and lower-income nations and healthcare systems), concurrent with a bottom-up education approach in the WHO's Digital Health Leadership Training Program (for healthcare workers and administrators in lower income nations, with the WHO coordinating the support of the UN's International Telecommunication Union, the U.S. Agency for International Development [USAID], and the German Deutsche Gesellschaft für Internationale Zusammenarbeit [GIZ]).

iii. Localized funding systems: Moving away from the traditional earmarked and donor-driven PubMed funding structures (in general and AI in particular) from the Global North to the Global South, there is a growing trend of direct fund transfers to PubHealth systems and governments for agendas devised at least in cooperation with if not led entirely by local systems and governments (Shamasunder et al., 2020). After long-standing anticolonial critique, sustained progress has been made by the Global Grand Challenges by the Bill and Melinda Gates Foundation and the Innovation Fund by UNICEF (United Nations International Children's Emergency Fund) in accelerating more local, precise, and collaborative, funding structures (including by 110 equity-free investments throughout 57 African nations) (Akogo, 2021). Partnership-based funding structures are also emerging including the Vietnam Ministry of Health's collaboration with the US Harvard Medical School and the Swiss pharmaceutical company, Novartis, to expand PubHealth integration with healthcare system's primary care focus (Shaaban, 2020). Governments from such emerging economies are increasingly investing in the PubHealth dimensions of their healthcare systems through AI-enabled digital health infrastructures (including through such private-public partnerships) as "joint wins" in both political and economical but also PubHealth dimensions.

4.6 AI health as healthcare system-based AI-PubHealth: sovereignty, solidarity, success

4.6.1 AI health conceptual update

This chapter has sought to fill out our understanding of how AI is enabling emerging PubHealth for the future's healthcare systems, with an emphasis on addressing its societal barriers to adoption (by emphasizing sovereignty and capacity-building) and technical barriers (by streamlining multisector data storage and analytics) which otherwise limit effective operation and system integration. As we progressively build to the future's AI-based thinking healthcare system, we can use the above AI-enabled PubHealth to update our previous model of AI Health (with an emphasis on how AI can help to automate and improve healthcare system decision-making for greater clinical effectiveness, costefficiency, and societal equity) (Monlezun et al., 2022b). Ultimately, the emerging AI-enabled PubHealth and healthcare system of the future we have increasingly been projecting, defining, and describing features not a single static solution to our historical healthcare challenges, but rather an equity-focused, value-based, AI-enabled adaptive model of the emerging model of the AI-driven or "thinking healthcare system" which we can now mathematically define below (Monlezun, 2022):

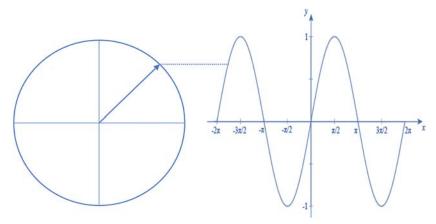
$$AI\ Health_{Mathematical} = \left(\text{HealthBD} \times \left[\overline{Delivery} + \right. \right. \\ \left. \sum_{n=1}^{\infty} \left\{ \text{PrMed cos } Delivery + \text{PubHealth sin } Delivery \right\} \right] \right)^{AI-VBHC}$$

AI Health is the Trustworthy deep learning AI Co-Design product of healthcare Big Data (HealthBD) and healthcare delivery, raised to the power of AI-enabled Value-Based Healthcare (AI-VBHC). Healthcare delivery as a periodic function is represented as the trigonometric form of a Fourier series as the infinite convergent series of the sum of the average unit of healthcare delivery at a patient level (as the average value of the function) and the summation of the cosine wave (of PrMed or Personalized Medicine) and summation of the sine wave (of PubHealth or Public Health) (Herman, 2016). The successive sum of these waves or harmonics (integer multiples of the periodic function's fundamental frequency) constituting the overall PrMed and PubHealth waves allows the convergence or increasing approach toward the limit as the function or number of terms increases (as the function y = 1/xconverges to zero as x increases). This healthcare delivery framework represents the operational function of healthcare systems whose central objective is to deliver VBHC, whose seminal definition earlier discussed was provided by Porter and Teisberg as a cost-benefit function of health outcomes achieved through quality healthcare divided by the per-person costs to achieve those outcomes (Porter and Teisberg, 2006). The European Commission's Expert Panel on Effective Ways in Investing in Health refined the definition of quality healthcare as consisting of equity, person-centeredness, social participation,

and wellbeing with implied safety (Smith et al., 2020). AI-VBHC specifically can be formulaically represented as:

$$\begin{split} \text{AI} - \text{VBHC} &= AiCE \times \left(\left[Clinical + Operational \right]_{AI} \right) \\ &\times \left(\frac{Quality_{Equity} \times Personal \times Social \times Wellbeing}{Cost_{Time} \times Capacity \times Support} \right) \end{split}$$

where AiCE represents AI-driven Computational Ethical and policy analysis. Graphically, a circle as the simplest shape can be represented as the sum of the trigonometric functions of sine and cosine below:



Similarly, the healthcare system in its operations can be represented as a circle created by PrMed proceeding forth as the cosine function from the fixed center of the patient-clinician encounter-relationship, the foundational unit of healthcare delivery. PubHealth is the sine function or internal limiting principle of PrMed, defining the limit of resource intensity at the individual level relative to what is permitted for the care of the population bounded by the healthcare system. Healthcare delivery with finite resources can thus be represented as the practical tension within healthcare policy strategically and healthcare systems operationally in a regularly shifting trade-off between individual-focused PrMed and population-focused PubHealth. For example, a nation or system with \$100 to spend on the 100 individuals under their care can spend \$90 for the 10 high utilizers (delivering big value to a small number) or \$90 for the 90 low utilizers (delivering small value to a big number). The research and operational implications of this framework are that AI-VBHC strategically and empirically transforms healthcare delivery from a zero sum to positive sum enterprise: instead of the predominant contemporary practice of shrinking one patients slice of the healthcare pie to expand the slice of

others, raising the above Fourier-based formula to the power of AI-VBHC expands the pie-the healthcare system becomes a more inclusive community as more patients can converge to efficient and equitable value healthcare by ensuring a regular adjustment to the trade-off, avoiding the sacrifice of a defined basic set of goods and services or value required for each individual. Because this is a convergent series mathematically, the algorithm operationalized version of this AI conceptual framework can increasingly approach and theoretically reach the optimal state or limit of value-based healthcare concurrently for individuals and populations (like in steady-state anesthesia where the concentration of a drug in a patient's body remains constant, achieved by real-time titration of the drug until the body absorbs it at the same rate it loses it).

In contrast to AI Health, the AI-driven Efficiency-Inequity Index (AI-EII) is represented as the ratio of PrMed and PubHealth, as the quotient of both of these harmonics mathematically defined as a divergent series (with more terms or positive unit fractions in the series adding to the partial sums of the series leading to the value of these sums progressively increasing and diverging away from a specific value) (Rice, 2011, pp. 269-276). Greater clinical efficiency delivering more effective outcomes in less time entails increases in populationlevel inequity as greater value is delivered for a smaller number at the expense of the many. This inequity has a two-fold dimension: resource inequity and societal inequity. Resource inequity refers to the disparities in the intensity of healthcare delivery (such as among 100 people, there may be 7 with significantly worse cardiovascular disease who develop ST-segment myocardial infarctions [STEMIs] requiring emergent and effective though costly hospitalbased percutaneous coronary interventions and post-cardiac rehabilitation). Societal inequity refers to the degree of disparities between observed disparities in health outcomes (along with the preceding process disparities in healthcare system access) and predicted outcomes (based solely on population distribution independent of non-medical causes of health outcomes). PrMed advances may initially produce significant benefit to a few, but such benefits theoretically should be diffused over time to the larger public (as those individuals have greater likelihood of health outcomes and improved productivity for society, and the advances in healthcare delivery may allow application for future patients). Technically, advances in AI-based PrMed may theoretically approach personalized PubHealth as PrMed to population scale allows as precise as possible tailoring of healthcare delivery (in prevention, diagnosis, treatment, rehabilitation, and palliation) to the larger population. Raising this ratio of PrMed to PubHealth to AI-VBHC helps achieve a more optimal balance of benefits for individuals and populations by increasing quality while decreasing cost, and structurally building this ratio into the above AI algorithm-based and human-curated model, avoiding any deliberate societal inequity increase with AI-driven system efficiency gains.

It should be here noted particularly within PubHealth that there is wide array of inequity indexes and metrics, including Quality Adjusted Life Years (QUALYs), Gini coefficient (in economics for health or income inequality), Health Equity Measurement Framework (HEMF) (provided a detailed quantification of social determinants of health), and the Population Health Performance Index (PHPI) (a single summary metric like Gross Domestic Product but for population health uniting mean and inequality health outcomes) (Klugman, 2010; Dover and Belon, 2019; Kindig et al., 2018). Yet even the most commonly utilized and accepted indexes and metrics face widespread criticism for excessive complex or questionable assumptions and modeling underperformance (relative to internal and external validity) (Van Mierlo et al., 2016; Olaiz, 2013). The 691 popular metrics for health inequities identified by a 2021 systematic review further supports the lack of general consensus about the optimal inequity metrics and their comparability across studies and programs, which only further undermines substantive research, healthcare system, policy, and societal progress improving equity (Albert-Ballestar and García-Altés, 2021). How can the future's healthcare systems improve health equity with AI if we do not know or agree how to define and measure equity?

Yet the greater challenge for such traditional approaches may actually be their static design-it cannot adapt, grow, nor "think" without significant human intervention, modification, retesting, and redeployment (which is inefficient and often ineffective, meaning we know the "right" thing in healthcare systems to do often long after the window for action closed). The AI Health approach particularly with AI-EII formally, technically, empirically, and structurally allows both short-term quantitative optimization and longerterm qualitative optimization. Short-term, the optimal tradeoff between PrMed and PubHealth can allow the AI-EII to approach 1 or maximum value (i.e., by 0.5 for PrMed and 0.5 for PubHealth). As AI-VBHC advances permit greater qualitative advances, PrMed can be increasingly done at scale to allow more precision PubHealth (and thus PrMed and PubHealth both approach 1 yielding an overall qualitative transformation of the index to achieve an outcome of 1). This can be seen as an AI-operationalized and thus modified version of the PHPI, but one that can adapt while being integrated with healthcare systems, improving itself as it digests more system data. AI Health with its emphasis on the relationship of PubHealth expanding the more equitable benefits of PrMed thus is meant to advance the future's healthcare systems toward achieving the WHO-stated "aim of AI4PH ... to maximize the benefits for society without compromising the rights of individuals" (Garcia Saiso and D'Agostino, 2021). It seeks to do so by providing a strategically sound and technically programmable formula to launch an AI that does not just "solve" the equation, but "thinks" through better solutions transparently (always under human supervision).

4.6.2 AI health: PubHealth's contribution to sovereignty, solidarity, and survival

Each of the previous chapters should be their own book to do justice to the material and people they touch, but they had to remain broad for our current journey in this book to give us a sufficient summary of the major concepts and trends in AI-enabled modern healthcare systems so we can productively dive into their detailed developments in the subsequent chapters dealing with the microdomains of telemedicine and patient safety and the macrodomains of politics economics and ethics (ultimately so we can reach a more defined, complete, and defensible vision of the future's healthcare system).

This chapter began by historically analyzing PubHealth's development from premodern quarantines to modern vaccines to 21st century global health to emerging AI-enabled partnership-based PubHealth, with the final step accelerated by COVID-19 demonstrating the field's design deficits particularly in insufficient collaboration and inequity. We considered the trends of digitalization, deglobalization, and demographic shifts framing the latest phase of this development and its emerging applications in PopHealth, precision Pub-Health, and system optimization. This brought us finally to consider AI Health as an operational design framework for the future's healthcare system that complementarily integrates PrMed (clinical + multiomics) with PubHealth (the ecological interface of healthcare systems + governments + societies) and raising it to the power of AI-accelerated value-based healthcare. The mathematical formula for AI Health additionally allows its digital transformation of AI-enabled healthcare systems with practical algorithmic translation (which we will increasingly explore in the subsequent chapters), not as a "rigid imposing roadmap but rather an inclusive formula for the future of healthcare systems that are effective, efficient, and equitable (by being automatable and adaptable for local communities' needs and values, rather than being dictated externally)" (Monlezun et al., 2022b). It provides the flexibility for each local community to adapt the inputs for their community's selfidentified needs, bounded by their own values (not being imposed as a onesize-fits-all telling communities how to go from A to B, but rather empowering them to seek their own self-determined destination of optimal well-being). Thus, an AI transformation of an ethically reimagined PubHealth in this emerging model of AI Health emphasizes sovereignty (of healthcare systems and states), safeguarded by solidarity for mutually assured survival rather than destruction. Such AI seeks to accelerate the effective and fair collaboration of governments, businesses, academics, community organizations, community members, and healthcare systems locally and globally (constituting the suprastructure of PubHealth)—to ultimately accelerate effective and fair health outcomes for individuals and populations. Accordingly, we now have a more refined conceptual foundation to examine the framework of the future's healthcare system through the lens of this AI Health.

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Chapter 5

Al + telehealth: plugging into the digital ecosystem

5.1 Telehealth overview

5.1.1 Conceptual framework

To start breathing life into the model of the future's healthcare system, let us make the conceptual framework of AI Health from the last chapter more concrete (by considering the clinical image of a person) and then applying it to the specific use cases of AI in telemedicine (telemed) and telehealth more broadly. One of the first classes for most medical students internationally (before they can graduate medical school as physicians) is anatomy and physiology. In this course, the clinical perspective of the person as a patient begins to take shape. Individuals can donate their bodies after death so future physicians can respectfully and systematically dissect, learn, and integrate their knowledge of how the form and function of the body unite to allow healthy operation of the body (and conversely illustrating how disease manifests disruption of these biological processes). AI Health applied to the model of the future healthcare system similarly can be conceptualized as a body: PubHealth structurally frames the "body" as its skeletal (sub-)system, telehealth and telemed serve as the tendons connecting PubHealth to the muscles of *PrMed* primarily moving the body forward; patient safety which we will see in the next chapter serves as the immune (sub-)system fighting external and internal threats (including harmful pathogens and excessive or dysregulated immune response); politics accounts for the respiratory or resp (sub-)system (as the healthcare system to function requires internal governance and external regulation according to consensus-based compliance with recognized authorities, themselves responsive to public demands); economics serves as its GI (sub-)system (as the healthcare system is fueled by funding, leading to operational "obesity" if overfunded and malnourishment if underfunded); ethics is the endocrine or endo (sub-)system (with feedback loops catalyzing and inhibiting processes to stay within safe limits according to widely accepted maxims of social behavior fundamental to healthcare system operations); HealthBD is the CV (sub-)system (uniting, oxygenating, and nourishing each of these organ (sub-) systems); and AI is the nervous (sub-) system "reading" how each of the above organs are doing and directing all the above processes. This clinical framework for AI Health thus is conceptually interchangeable with the previous chapter's mathematical formulation (with the remaining elements outside of PrMed and PubHealth empirically captured as inputs and outputs for them):

$$\begin{split} AI \; Health_{Clinical} &= \left(Skeletal_{PubHealth+Tele} + Muscle_{PrMed} + Immune_{Safety} \right. \\ &\left. + Resp_{Politics} + GI_{Economics} + Endo_{Ethics} + CV_{HealthBD} \; \right)^{Nervous_{AI}} \end{split}$$

Within this organic healthcare system model, let us drill down to see how telehealth illustrates and facilitates the interdependent and complementary functioning of the operational pillars of modern systems (PrMed and PubHealth). The prior chapter explored how PubHealth is constituted by the suprasystem structure connecting governments, academics, community organizations, and healthcare systems while concurrently (at the level of the healthcare systems) operating through the above actors (with notable but not equivalent overlap with systems' most PubHealth-like functions manifested by PopHealth). Systems principally move through PrMed (and its increasingly precise clinical medicine) at their most fundamental and discrete unit of the provider-patient encounter, within the larger PubHealth network of actors influencing and influenced by this fundamental unit of systems operation. Accordingly, PubHealth helps illustrate the organic organization (not completely centrally nor deliberately planned) "natural" network of actors which converge operations to the extent of aligned interests, scope, and supply chains (which digitally AI-HealthBD broadens their traditional boundaries and deepens their interdependent functioning beyond just the hospital walls). Such broadening is seen with the previously explored pandemic mitigation measures, for instance, which require healthcare systems to collaborate for the larger health of the global human family, while simultaneously concretely manifesting this PubHealth structure through such collaboration. Telehealth as we will explore shortly strengthens the connection between PubHealth and PrMed by deepening the interdependent functioning of the latter two.

Specifically, this chapter will explore telehealth terminology (what differentiates it from telemed), post-COVID-19 surging investments and regulation, disparities and developments in its adoption (focusing on connectivity and digital health infrastructure), collaborative intelligent connectivity (spanning AI, IoT, 5G, and space), AI telehealth use cases, and telehealth's emerging streamlined integration with healthcare systems (including how value-based healthcare and geospatial analytics inform this integration). Telehealth matters increasingly to healthcare systems (especially following the emergence of the COVID-19 pandemic) because of its increasingly demonstrated advantages of offering cheaper, easier, faster, and fairer healthcare

delivery and augmentation of it (claims we will analyze in the following sections). And AI is serving as the force multiplier for these advantages, along with its mechanism for sustainable integration with the healthcare system through the larger HealthBD infrastructure and system operations.

5.1.2 Telehealth = eHealth + telemedicine

To clear up common terminology confusion, telemed is formally defined by the U.S. Federation of State Medical Boards (FSMB) as "the practice of medicine using electronic communication, information technology, or other means between a physician in one location, and a patient in another location" in a way that may or may not include an "intervening health care provider" (FSMB, 2018). The WHO specifies "eHealth" is broader than telemed for it refers to the "the use of information and communication technologies (ICT) for health" (WHO, 2005, p. 121). Both telemed and eHealth are components of the overarching "telehealth," which the U.S. HHS defines as "the use of electronic information and telecommunication technologies to support and promote long-distance clinical health care, patient and professional healthrelated education, public health and health administration" (HHS, 2022). "Telecommunications" denotes "the means of electronic transmission of information over distances," typically networking together diverse information systems (ranging from sounds [including phone calls], texts, images, and videos) often through storage, analysis, and transmission by integrated computer systems through electromagnetic systems (Laudon and Traver, 2011). Computers "talk" to each other through discrete digital signals (0 and 1 values) such as listening to satellite radio in the car, in contrast to the alternative electromagnetic wave of analog signals (infinite possible values varying by frequency and amplitude) as through standard radio stations. You are using telecommunications therefore every time anyone communicates anything to you other than in person, leaving telehealth to constitute the vast majority of the healthcare delivery pipeline and network (as the majority of healthcare services and products are delivered outside the provider-patient face-to-face in-person encounter). Most of what affects our health and how we address it occurs outside of the clinical exam or hospital room with the provider, meaning that telehealth is growing in importance and utility (especially as the healthcare overview chapter detailed the emerging model of the future's healthcare system moving to the newer adaptive patient-home-centric ecological model in contrast to the older rigid provider-hospital-based traditional model). As AI increases system efficiency and societal focus on equity, telehealth is also particularly emphasized through strategies and operations to reduce disparities in healthcare access particularly for minority, poor, and rural populations.

5.2 Post-COVID surging usage + investments

As we explored in the PubHealth chapter how COVID-19 accelerated a global pivot and push to more effective and equitable solutions, telehealth similarly has become a key tool toward this vision. COVID added fuel to the preexisting trends of growing demand by patients (for more convenient and consistent access) and healthcare system and payor pressure (for more affordable operating costs). These costs include upwards of 2 of every three ED visits which are not only avoidable (and not actual medical emergencies so can be treated outpatient by PCPs) but are also 12 times more costly than PCP visits (UnitedHealth, 2019). Taken together, approximately a quarter of a trillion dollars annually in the United States alone may be shifted to telehealth for more efficient care.

These underlying forces are increasingly driving up telehealth usage and investments. U.S. data indicate that just 11% of people in developed nations prior to the pandemic used telehealth services, but following the pandemic's first 2 years, the number of those interested in such services has leaped by 76% (with 57% of providers now viewing it favorably as telehealth usage increased by 38 times from January 2020 to February 2022—and remaining at least at such levels for a solid year up to the most recently available data) (Bestsennyy et al., 2021). The U.S. telehealth market is expected to continue to grow at least an additional 28% through 2026, driven by increased postpandemic demand, healthcare system acquisitions and collaborations of telehealth vendors, reimbursements, and telehealth robot and robotic platforms (automating entire segments of care) (Arizton, 2021). This expansion is projected alongside the \$51 billion profit growth in virtual urgent care services, remote patient monitoring (including remote device and clinical variables), web and appbased services, and cloud-based infrastructure. Such expansion is expected from the United States outwards to particularly lower-income nations able to leverage the lower-cost telehealth services for enhanced medical care access for their populations (augmenting their local in-person providers and healthcare centers). These advances are fueled not only by patient, payor, and provider demand, but also by the private business sector which notched a 300% increase in venture capitalist digital health investments from just 2017 to 2020 (Krasniansky et al., 2021). Globally, the record for highest telehealth funding quarter was set by the first quarter of 2021 up to \$9 billion (following the pandemic's first year), nearly double from the prior year (with North America and Europe outpacing other regions), concurrent with more digital health companies ranging from multiomics to consumer health foci moving from private to public ownership through SPACs (special purpose acquisition companies) and traditional IPOs (initial public offerings) as government, industry, and healthcare system stakeholders increasingly share the shared projection of telehealth as a core healthcare system asset becoming a longterm consequence of the pandemic (CBI, 2022). Aside from telehealth, the

other surging sector of healthcare emerging from the pandemic is AI with a 140% jump in investment from the first quarter 2020 to 2021 up to \$2.5 billion in the first quarter alone (with much of these investments backing companies providing support services to better enable telehealth). For instance, the MLbased payment platform, Cedar, raised \$200 million (to assist providers communicating through personalized messages with their patients), as Strive Health bagged \$140 million (to integrate telehealth remote monitoring and prediction of kidney disease through integrated demographic, clinical, claims, and dialysis machine data), and Infinitus Systems raked in \$21 million (to automate provider phone calls to patients).

In parallel with healthcare systems seeking to build their internal telehealth capacities, industry stakeholders are also building their capacities to take advantage of such growing telehealth usage and investments by serving single healthcare systems either as partners or as acquisitions, including CloudMD Software and Services, Veeva Systems, 1LifeHealthcare, Teladoc Health, and Allscripts Healthcare Solutions (FN Media, 2021). Though we will explore in more detail some of their emblematic use cases through healthcare system integration shortly, we will just note here how usage and investments are synergistically growing telehealth as a strategic core asset for healthcare systems with the example of CloudMD. This comprehensive telehealth online platform integrates an online patient portal, cloud based EHR, medical billing, and revenue management systems spanning over 5700 providers (PCPs, nurses, and mental health professionals) and 12 million patients (mostly in Canada and the US), with expansion continuing to Mexico, Nicaragua, Costa Rica, and Panama (initially through the access of its educational database extended through Apotex Latinoamerica) (CloudMD, 2022; FN Media, 2021). Even after the emergency phase of the COVID's first 2 years, CloudMD has continued the ride the telehealth growth wave with a 372% year-over-year revenue jump as telehealth companies increasingly are positioning themselves to attract significant public and private insurance payor, private industry, and direct healthcare system investments by becoming an integrated and online "complete healthcare ecosystem," able to agilely plug into healthcare systems across diverse regions to augment systems' capacities and fill unmet needs (Salunkhe, 2022). Telehealth accordingly is bypassing the most expensive costs of healthcare systems (personnel and buildings) to deliver direct patient-centric healthcare (maximizing provider time online) while providing varying degrees of seamless integration with healthcare systems (through streamlined EHR and billing platforms), with the added online convenience and access spanning wide geographic stretches. Accordingly, telehealth innovation has grown with such services by and in partnership with healthcare systems to include virtual urgent, chronic, and hybrid (augmenting in-person) medical care to increase patient access, convenience, affordability, and outcomes.

5.3 Digital ecosystem: disparities and developments in health infrastructure and regulations

5.3.1 Global digital ecosystem

Telehealth accounts for one of the densest and most operationally intensive dimensions of the digital health (sub-)ecosystem within the larger global digital ecosystem. To better understand telehealth and its AI-enabled applications, we will first seek to understand these ecosystems in more detail first. An "ecosystem" is traditionally defined as a complex network of relationships between living organisms and their physical environment, joined by the nutrient and energy cycle, restricted to a specific space, and orientated to the ultimate goal of survival of the organisms (Bergmann, 2021). The term was increasingly applied in the later 2010s in economics as a paradigm shift considering firms no longer predominantly as solitary actors but rather as members of larger interdependent and connected networks (concurrent with and similar to the transition from PubHealth to global health) (Jacobides, 2019). These economic ecosystems began denoting "orchestrated network[s] spanning multiple sectors" consisting of firms who "shared standards ... to make their products and services compatible" and so complementary valueadd, boosting their competitiveness for consumer demand. Like in organic ecosystems, firms like organisms in this paradigm influence and are influenced by their larger economic context and seek competitive advantage to survive, including when mutually beneficial relationships aide this ultimate goal. These artificial or "designed ecosystems" were a direct result of the Fourth Industrial Revolution. Digitalization accelerated the integration of diverse sources of data, fueling the tighter integration (and bundling) of firms and their products and services. This in turn fed and was fed by deregulation and technological trends of increasingly "complex and customizable product-service bundles." This grouping required more interdependent relationships between firms and their related supply chains to resource such bundles for growing global demand. Digitalization helped broadened our understanding of how we are connected, AI made this surge in data understandable and actionable, and the shortcomings (and even failures) of healthcare falling short of responding to patients' needs (discussed in the preceding chapters) aided the shift of this digital ecosystem into traditional healthcare systems.

5.3.2 Digital health ecosystem

Telehealth growth rode the wave of healthcare systems as digital ecosystems by digitally expanding the limits of systems from the material walls of hospitals to wherever the patient is. Accordingly, the paradigm shift in healthcare to understanding this economic sector as a supraecosystem (in addition to being a network of ecosystems of interconnected healthcare systems) began in

the later 2010s providing increasingly the three strategic benefits of access, scale, and adaptability (Pidun et al., 2021). Healthcare systems aligning themselves with other systems and stakeholders have greater access to a greater range of capacities, which traditionally had been denied them because of cost and time constraints (i.e., you do not have to build or buy what you can share). Such specific healthcare ecosystems additionally could scale more rapidly than the historical model of healthcare systems seen as pipelines built on a growth process that was strictly linear; instead, systems could now grow nonlinearly and modularly by adaptively scaling up or down capacities through strategic collaboration with other stakeholders (similar to the larger "shared economy"). And amid the uncertainty and unpredictability of healthcare systems (think how COVID disrupted the entire sector [particularly systems' PubHealth operations] with little to no warning), healthcare ecosystems can infuse systems with agile resilience by enabling adaptation to unfolding technological innovation and consumer needs.

The strategic trends driving the transition of traditional healthcare systems to more digital health ecosystems (with telehealth central to digitally expanding systems' walls to better encompass patients) encompass increased ecosystem advantages, patient demand, supplier competition, technological connection, and eased regulations (Pidun et al., 2021). COVID arguably provided not only a compelling global demonstration of the inherent structural failings of the traditional healthcare system model but also the unique advantage of telehealth and related core features of the digital health ecosystem to enable the survival of the emerging healthcare system of the future. Telehealth pushed the reach of traditional systems into patients' homes, workplaces, and communities on-demand and contact-less through their mobile devices, particularly as patient demand for remote and convenient access (similar to other nonhealthcare sectors) surged amid widespread societal lockdowns to reduce the viral spread in public places. Nontraditional suppliers also have increased their competitive push into telehealth including Apple, Microsoft, Amazon, and Google (fighting for greater market share of healthcare cloud services) and even Walmart (linking outpatient clinics with their large geographic footprint in their stores), triggering healthcare systems to reinforce their telehealth offerings for patients to retain their business. The AIenabled digital integration of the IoT within the Fourth Industrial Revolution facilitates the above trends as telehealth becomes faster, easier, and cheaper including not only for established stakeholders like the above but also for new start-ups. And finally, government regulation easing allows an increased number of nations to allow more stakeholders, services, and reimbursement for telehealth providers (including more concrete and streamlined guidance particularly in Australia, China, Indonesia, Japan, European Union, Saudi Arabia, North America, Brazil, Argentina, and Chile) (Bodulovic et al., 2020).

The practical drivers allowing healthcare systems to transition into AIenabled and telehealth-empowered digital healthcare ecosystems center on

5.3.3 Digital health infrastructure + telehealth blockchain

The successful precursor model for digital health infrastructure is SWIFT (The Society for Worldwide Interbank Financial Telecommunications) which was created in 1973 from 239 banks stretching across 15 nations, forming an early banking ecosystem that has since become the dominant global financial language and messaging service (Scott and Zachariadis, 2014; SWIFT, 2022). A standardized SWIFT code is assigned to financial institutions including banks which allows international payments to be made, validated, and routed through

user front-end platform. Such cloud-based digital infrastructure integrates these data streams from its various contributing actors (i.e., patients, providers, social media and community actors, and financial firms) to produce a more complete understanding of the patient-user and the larger patient populations.

a single automated computer system stretching even across complex networks of intermediary institutions regardless of nationality or language, allowing the contemporary digital infrastructure to join over 11,000 institutions from over 200 territories and nations. A growing number of healthcare systems are similarly building out their digital health infrastructure in their transition into telehealth-anchored digital health ecosystems. (a) Open application programming interfaces (APIs) and (b) US HHS interoperability updated rules are steps in this direction.

- (a) An API is a set of digital rules acting in an intermediate layer between web servers and applications facilitating data transfer between systems to allow diverse actors to communicate with each other in the data and functionality of their products and services (IBM, 2020). Like a bank transferring a payment to a different bank on the other side of the world through SWIFT, a firm's application can initiate an API call (through its Uniform Resource Identifier [URI]) that requests an external web server's data, the API then transfers the request to the server, the server responds by sending the requested data to the API, and the API in turn transfers it to the original requesting application. The U.S. 21st Century Cures Act mandated healthcare systems provide patients access to their EHR records through patient-facing APIs without prohibitively difficult access (CMS, 2015). And yet 5 years later only 8 of 10 of the leading HIT-adopting systems have such APIs (Neinstein, 2020). Persistent API adoption barriers include data security, technological and regulatory immaturity (with prohibitively lower functionality and specification of approved products and services), EHR vendor's incomplete data sharing, and insufficient funding. Yet there are emerging advances in contemporary telehealth actors using APIs as a form of shared digital platform (i.e., messaging or data transfer network) in digital health ecosystems to create more effective digital infrastructure bridging even 6+ multi-cloud architectures each with their own cloud platforms across multiple actors (iPatientCare, 2021).
- (b) The U.S. CMS sought to advance digital health ecosystems' data interoperability amid these challenges with its May 2020 Interoperability and Patient Access Final Rule by specifying and mandating supposedly streamlined policies and standards for secure data exchange among patients, providers, and payors (CMS, 2020). It required CMS-regulated payors (collectively accounting for the largest U.S. healthcare funders covering approximately 90 million patients) to use the Health Level 7 Fast Healthcare Interoperability Resources as the national standard for API technical framework, in addition to the data liquidity content and vocabulary standards. CMS went so far as to mandate a certain density and frequency of data exchange among actors in healthcare systems' digital health infrastructure to supposedly advance the effectiveness and efficiency of such infrastructures as the backbone of ecosystems. Yet the rule

explicitly acknowledged the challenges to better improving and operationalizing this infrastructure particularly for telehealth (namely, the lack of healthcare sector consensus on digital standards, including certification criterion for patient event notifications). Essentially, the development of health digital infrastructure is challenged technically and societally—it can adopt the innovations of digital infrastructures from other economic sectors to become more efficient, yet widespread societal pressure understandably grows for protecting data security and privacy. Such trends translate into often prohibitively complex or slowly rolled out (even sometimes conflicting) regulations for what constitutes shareable data and how that data can be shared and with whom.

A notable emerging development in digital health infrastructure to address such challenges (with particular relevance for telehealth) is blockchain. The subsequent sections will more fully discuss the IT architecture for telehealth and the following chapter on patient safety will analyze blockchain within it in particular. But prior to that, it should be noted how there are growing innovations to the fundamental structure of the overarching digital health infrastructure including blockchain technology adapted from other economic sectors. Healthcare blockchain refers to a digitally distributed and decentralized data infrastructure or computer network utilized to securely and confidentially manage a shared ledger of multiple individuals' health records (in which each node [device or server] within the chain stores verified, synced, and secure copies of the ledger) (Ahmad et al., 2021). Unlike traditional datasets which typically store data in tables often controlled by a single body (susceptible to fraud and hacking), a blockchain is structured according to blocks of chronologically grouped data (with new blocks created and linked to previous ones once their storage capacities are reached). As such healthcare blockchain particularly in telehealth can uniquely enhance sensitive health data's privacy, security, health records immutability, fraud monitoring, and operational transparency by embedding decentralized data security and integrity throughout each node constituting the blockchain.

5.3.4 Regulations

The major rate-limiting step for telehealth's further adoption by healthcare systems may be less the science and more its applications (infrastructure as noted above and regulations noted below). Since the healthcare sector lags other economic sectors in digital technology adoption (as already noted previously amid the traditional societal caution with the more sensitive health data), there are concerted global efforts to reduce regulatory barriers. The CMS attempt above is an emblematic step in this direction that interestingly injects a dimension of "encouraged growth" into the historically restrictive dimension predominating in regulations. They usually focus on what

healthcare actors cannot do, not what they can (and should do). Such a more activist-like application of regulations is seeking to therefore catalyze the transition of traditional healthcare systems through the intermediary step of greater telehealth adoption to the ultimate strategic step of becoming successful digital health ecosystems (competing on equitable value-add for patients and populations). Growth-orientated regulations can be divided according to (a) reimbursement and (b) innovation.

- (a) Nearly 1 in 4 of the leading international healthcare actors cite limited telehealth reimbursement as a major barrier to investment in their digital infrastructure (and a leading barrier overall), though 64% of these leaders are aggressively investing in telehealth regardless given the long time horizon on realizing a return on the investment, the current heated talent grab, and the optimism that reimbursement will improve eventually (Kimpen and Wiegand, 2021). Governments and payors from multiple nations particularly the U.S. boosted pandemic-era reimbursements for telehealth (to be on par with office visits), significantly increased the number of services reimbursable under the physician feed schedule (more than doubling in the case of the United States), permitted virtual visits to substitute for the first primary care consultation (notably in the Netherlands), and lowered or eliminated site restrictions (allowing telehealth to reach beyond its traditional boundaries of rural and underserved regions) (CMS, 2022; CMS, 2021; MTRC, 2020).
- (b) COVID-19 accelerated unprecedented widespread and rapid telehealth innovation (in weeks compared to the usual years-long process) as governments slashed regulatory barriers to telehealth expansion to compensate for healthcare systems' inability to keep up with explosive pandemic-era telehealth demand, while navigating often societal widephysical distancing mandates (Kimpen and Wiegand, 2021). Such competitive innovation (with the minimal required regulation to optimize safety in created healthcare products and services) has been a growing focus of the U.S. FDA, exercising one of the world's most influential body of regulations given its history (guiding UN, WHO, and FAO standards for international trade of drugs and food), economics (regulating the largest regional portion of the global healthcare sector which is centered in the United States), and politics (as most of the supply chains for US-based healthcare actors stretch internationally and so require the FDA's Foreign Offices) (Abram and Abdoo, 2021). Balancing the competing pressures for innovation and safety, the FDA has increasingly sought to empower the healthcare sector to operate with maximal possible latitude by stimulating greater efficiency and agility in AI-enabled telehealth R&D, as evidenced by its seminal and emblematic authorization of marketing AI in cardiac ultrasound use (Muoio, 2020). This is notable because of the template type of regulatory framework of the FDA and the related

implications of this approval. The FDA enumerates principles for a particular type of healthcare product or service in its template or initial approval for the early case uses which then guides subsequent approvals. And in the AI cardiac case of Caption Health, the technology use was expanded to nonexpert medical staff such as nurses in a primary care clinic (diffusing the benefit of advanced diagnostics to even those unable to access the traditional experts in such diagnostics). Subsequent approvals similarly have advanced attempts to define the minimum safety standards and processes to extend healthcare delivery via telehealth amid provider and resource limitations particularly for underserved communities.

5.4 Bridging telehealth's digital divide with edge computing

5.4.1 The digital divide's threat to disparities and telehealth

The UN Secretary General António Guterres during the initial emergency phase of the COVID-19 pandemic declared the "digital divide" is not only a "matter of life and death" for the societally disadvantaged (less able to access digital technologies, particularly the internet), but also may "become the new face of inequality" (Guterres, 2021). As telehealth is among the leading drivers of healthcare systems' digitalization and related AI-facilitated structural transformations, telehealth increasingly risks accelerating the digital divide's perpetuation and exacerbation of societal disparities (and the operational inefficiencies hampering telehealth's development) (Velasquez and Mehrotra, 2020; Valdez et al., 2021). Decreased access and literacy with the internet and such telecommunications as video chat that are more pronounced among racial minorities, rural residents, and lower-income communities can translate into exponential worsening of overall healthcare outcomes as systems are increasingly digitized, driving increased calls for the digital divide to be considered and addressed as a key social determinant of health (Clare, 2021). Aside from the strategic, economic, and ethical pressures of nations and healthcare systems to reduce such disparities in telehealth and thus improve value overall, the digital divide can threaten the survival of telehealth and weaken healthcare systems by undermining telehealth's economies of scale and systems' financially efficient population health management (Farmer, 2020). Worsening healthcare provider labor shortages (particularly in poor and rural communities) can increase the need for telehealth while undercutting its funding—as system access shrinks, sicker, and thus more costly patients can require more inpatient and resource-intensive care (that subsequently reduces systems' budgets for telehealth, while straining more profitable healthcare centers and thus their own telehealth funding, including infrastructure and

functionality development). The sum total of the above can weaken the economies of scale otherwise that telehealth could realize (by making its services more affordable for more patients by spreading the overhead development and deployment costs over more patients and payors, reducing input costs while increasing output size) (Bernet and Singh, 2015).

The WHO in their landmark 2018 resolution (a telehealth and digital health milestone) underscored the importance therefore of such ICT as digital healthbased telehealth to advance toward the UN sustainable development goals (SDGs) (WHO, 2018). The digital divide is so fundamental a challenge to the modern world rapidly and rampantly being transformed by the Fourth Industrial Revolution that the UN Conference on Trade and Development (UNCTAD) is considering going so far as to designate internet connectivity as a basic service (practically on par with food, water, and shelter) (Makri, 2019). Without it the societally disadvantaged are increasingly cut off from and left behind the digital-run world (and thus healthcare systems) including from resources, education, jobs, and especially healthcare (as lower income and less digitally connected communities are more prone to having lower physical access to fewer number of healthcare facilities staffed by lower numbers of providers and health technology and specialty expertise). This divide accordingly segregates 45% of the global population as of 2018 (with 80% of individuals in the least developed nations having internet connectivity and rural communities having one-third of the internet usage of urban regions). Yet there was a 347.83% surge in mobile phone subscriptions per 100 residents internationally from 2005 to 2018 (reaching 95% phone coverage worldwide with the exception of sub-Saharan Africa), which is particularly notable given it is the only means of internet access in much of the world. From the Congo's Ebola outbreak to Vietnamese HIV testing, the digital divide continues to illuminate real time and widespread improvement or worsening of healthcare disparities.

The world's largest telecommunications trade organization representing mobile network operators, the Global System for Mobile Communications Association (GSMA), defines the divide between the coverage gap and the usage gap, depending on whether individuals fall outside of the reach of mobile broadband networks versus have decreased access to such networks (GSMA, 2018). The correlative dimensions of the larger digital divide are considered to be the service-delivery divides (in equitable access to sufficient network infrastructure) and service-fruition divides (in equitable digital literacy and personal capacities such as handicaps challenging infrastructure use), which AI-enabled edge computing in the emerging phase of IoT appear increasingly well positioned to improve telehealth and its related disparities (Suraci et al., 2022). There is growing profit incentivization for government, business, and healthcare stakeholders in the digital health ecosystem for such

technologies as current projections indicate that up to two-thirds of the global population may have internet access by 2025 concurrent with a \$2.5 trillion GDP boost by 2030 from such digital technologies (as the pandemic alone drove a 19.6% increase in data traffic).

5.4.2 Cloud-fog-edge computing in IT architecture

Before we get to AI-enabled telehealth edge advances, let us first clarify what edge computing is and how it is shaping the emerging phase of the IoTpowered Fourth Industrial Revolution (remaking the digitalization of healthcare along with all major economic sectors). Going back to the prior chapters' discussion on clouds, these data infrastructures are subcomponents of organizations' larger IT architecture (which consists of the major components of technology architecture [with its subcomponents of the cloud data infrastructure and its underlying linear subcomponents of data streams, integration platforms, and software elements] and functional architecture [with its subcomponents of applications [interfacing with the above software elements] and functional capabilities) (Widjaja, 2020). "Architecture" traditionally has referred to the design of a building that informs its construction to achieve esthetic and structural-functional objectives (Collins et al., 2021). Therefore such an IT architecture generates and orders the infrastructures of its subcomponents to communicate, manifest, and potentially even achieve certain esthetics and functions identified as key to an overarching digital vision and related objectives (usually to advance organizations' missions of producing their niche products and services, augmented by digitalization facilitating the communication of information latent in such processes). Within this architecture, edge computing refers to the distributed computing framework bringing data storage, networking, computations, and related functions closer to the digital "edge" (of the digital world generally and IT architecture specifically where users interface with the architecture and generate data, particularly through IoT devices like smart phones).

The IT architecture can be conceptually represented hierarchically more simply from the perspective of IoT users (and thus data flow) by seeing it as cloud, fog, and edge infrastructure (and related computing) (da Silva and da Fonseca, 2019). Because it is closer to edge users than the cloud, the fog layer can reduce cost while reducing data processing delays and thus latency (milliseconds in response time after starting a network request such as trying to connect via WiFi to the internet on your smart phone), including for devices with different latency requirements. Nodes are the fundamental units of layers, i.e., a fog node may be a network device that communicates with cloud servers to coordinate their underlying edge devices. In the digital world, speed and functions are (nearly) everything. Fog and edge computing are experiencing explosive investment and attention as up to 75% of global data by 2025 is expected to be processed outside of traditional cloud data centers (as the

functionality of IT architecture moves increasingly to more localized, realtime, point-of-care, or use by end users using more swarm or clusters of data processing servers and networked devices) (van der Meulen, 2018). The Global Datasphere, the quantifiable description of the global digital ecosystem (in terms of how much and quickly data is created, replicated, and stored), is projected in that same time period to expand by over 430% as the physical world is digitized, leaving upwards of 49% of the planet's data stored on public clouds (with integrated fog and edge computing required to allow users to meaningfully engage with them)—this is so large that if you could download the entire Datasphere at current U.S. average internet connection speed, it would take you 1.8 billion years (Reinsel et al., 2018).

In this environment, cloud (large public, private, and hybrid), fog (remote noncloud servers, cell towers, branch officers, data gateways, and microdata centers), and edge particularly endpoint elements (i.e., phones, remote sensors, personal computers, APIs, and connected cars and robots) (Reinsel et al., 2018). Telehealth is therefore rapidly benefiting from such edge and fog computing extending the cloud's access and functionality for users in this emerging phase of the Fourth Industrial Revolution as greater edge intelligence enables patient and diagnostic devices to more time and cost efficiently collect, analyze, and make recommendations based on patient data while propagating such data through fogs to clouds which then communicate back to the edge (usually confirming or fine-tuning the analytics and recommendations). And this trend toward greater edge utilization to increase telehealth effectiveness and related disparities is expected to only continue. Consider how the energy sector is among the most digitally driven (turning digitalization into intelligent decisions, while healthcare is among the least such intelligently digitized sectors), and yet a traditional offshore oil rig uses less than 1% of its 30,000 sensors to make management decisions (Manyika et al., 2015). The space to grow remains big and wide.

5.4.3 Edge telehealth reducing disparities

How can edge-enabled telehealth improve patient outcomes including disparities? Economies of scale can be achieved by expanding the geographic reach of telehealth (particularly multistate including in the case of rural and minority populations), reducing the costs for patients while expanding their healthcare access (concurrent with increased profit for telehealth vendors and telehealth-enabled healthcare systems as the costs are lower and revenue higher as expansion increases) (Yilmaz et al., 2019). But this expansion can reach technical barriers with the service-delivery and service-fruition dimensions of the digital divide, which edge computing is uniquely suited to mitigate. The most notable advances thus far are occurring with focused applications on discrete technical problems, especially with ML embedded in edge endpoint devices in telehealth networks (connecting remote patient portals with clinic providers and hospital-based providers [in the data propagation gradient from the edge to fog to core infrastructure within healthcare systems' IT architectures]) (Suraci et al., 2022). Such edge AI can not only facilitate greater functionality by each device for edge users of telehealth, but also improve self-organization, adaptability, and data communication of edge devices even to the point of adaptive automation (Saad et al., 2019; Hidalgo et al., 2020; Chen et al., 2019; Pisoni et al., 2021). Devices can respond to the relative needs of other local devices and support and modify the distribution of network resources to match demand with supply in real-time (in terms of data storage, processing, computing, prediction, and ultimately functionality). Edge AI therefore has been utilized in such use cases as identifying socioeconomic drivers of the Spanish digital gap, in addition to informing adaptive distribution of network resources based on user behavior (even using single edge [and fog] nodes to communicate data on user disparities and connectivity to the rest of the network) and personalizing the edge experience of the traditionally digitally excluded (including based on culture, advanced age, and disabilities).

AI-enabled edge improvements are particularly key for such telehealth applications as remote surgery (where robotic and allied health professionals at the point of the patient assist with conducting procedures while the surgeonphysician is at a different location) and motor rehabilitation such as with stroke patients using virtual reality (VR), while prioritizing reliability, security, and latency (Senk et al., 2022; Wang et al., 2022). The latter two examples can allow remote and underserved populations to access procedures and rehabilitation which they otherwise may struggle to do so (while noting the utility of such telehealth services can be prohibitive if not sufficiently enabled by edge computing with sufficient speed and safe reliability). AI-empowered edge-toedge devices including hospital equipment (including wheelchairs and beds) fitted with remote sensors along with patients' home sensors can respectively allow more efficient equipment management (reducing waste, cost, and time with more adaptive and leaner inventory management and related patient transportation and care) and disease prevention (allowing cheaper home monitoring, reduced hospitalization length of stay, and earlier warnings of disease progression through shifting the care that can be shifted from hospital to home) (AT&T, 2018). This end-to-end networking allows IoT endpoint devices to more rapidly communicate and act in unison with other devices without requiring clouds or cores to the same extent historically required. Thus, as AI accelerates the capacity for improved edge and fog computing extending traditional cloud infrastructure, healthcare disparities can be particularly improved as systems' enhanced IT architectures allow telehealth to reach patients behind the digital divide on the digital periphery (as nodes there can inform continual adaptive network performance supporting increasingly efficient financial and clinical operations by healthcare systems for such underserved populations).

5.5 Bridging telehealth's digital divide with Al-enabled collective intelligent network connectivity

5.5.1 Connectivity disparities

A digital health infrastructure can be seen as a useless and "lifeless" digital skeleton, without sufficient internet and intelligent connectivity animating it (and helping bypass its challenges noted in the above sections). As the Pub-Health chapter discussed, this dual connectivity is key to healthcare system's fundamental readiness to ultimately deploy healthcare AI in general and AIenabled digital infrastructures for telehealth in particular (Ghebreyesus and Swaminathan, 2021). Much of the telehealth developments (in research, development, funding, and regulations) have been in higher-income nations to increase the profit of the already profitable healthcare sector and its systems, though the greatest benefit of telehealth may actually be in lower-income nations. The WHO therefore highlights how digital disparities in connectivity challenge the otherwise higher quality and lower cost telehealth services which could at least theoretically reach underserved communities to improve their health outcomes and related equity (remotely diffusing health knowledge and resources that are traditionally concentrated geographically in higher income systems and states compared to their lower-income counterparts). The previous section discussed how healthcare systems' IT architectures boosted by edge computing can more efficiently serve patients (particularly those socially disadvantaged). Yet this leaves unaddressed how can patients benefit from such technologies if they cannot even connect to the internet. From the first days of the pandemic up to December 2021, the UN noted a 17% jump in internet connectivity (or 782 million additional users) with the "COVID connectivity boost" following widespread lockdown measures across systems and states, the fastest growth in over a decade (Jacobson-Gonzalez and Albertini, 2021). Though nearly all of this impressive growth was in developing nations, 2.9 billion people globally (96% of whom live in developing nations) still face steep barriers to accessing the internet (and thus such advances as telehealth). The burden of this connectivity divide is disproportionately borne by women, minorities, rural residents, and older individuals. How can the divide be further reduced?

5.5.2 Nonterrestrial networks

Non-terrestrial networks (NTN) garnered international attention in February 2022 with the US-based SpaceX corporation sending over 10,000 Starlink NTN terminals to Ukraine following Russia's invasion and systematic destruction of civilians and civilian infrastructure (particularly telecommunications) (Wadhwa and Salkever, 2022; Blinken, 2022). In just the first 2 months, the terminals brought 590 hospitals and clinics back online to allow their continued operations internally and coordinating externally among the war-torn nation (helping manage resources and transport civilian patients for life-saving treatment). These NTNs are just 23 inches wide, mobile, and resilient to Russian cyberwarfare attempts to compromise them, unlike cellphone and transmission towers which were largely wiped out quickly from intense bombardment and shelling. Such NTNs are part of larger global efforts to decrease the service-delivery dimension of the digital divide through airborne and spaceborn networks enabling reliable continuity and scalability of internet connectivity, particularly in remote, emergency, and crowded situations (where traditional terrestrial broadband networks have largely failed) (Suraci et al., 2022). These geostationary (i.e., unmanned aerial vehicles [UAVs]) or orbital satellites (at low or medium orbit) can be assembled as a swarm, cluster, or mega-constellation consisting of numerous small devices scaled up or down based on user needs. NTNs paired with the larger digital health ecosystem can thus help expand real-time, higher-resolution remote monitoring, medical imaging, remote robotic surgery, and videoconferencing (Michailidis et al., 2020).

5.5.3 Al-enabled connectivity

There are increasing applications utilizing AI to integrate NTNs and edge computing to overcome the classic spaceborne telecommunication hurdles (limiting their cost-efficient connectivity improvements for organizations' telecommunications networks) including power allocation, energy consumption, and computing offloading. In particular, DL-enabled edge intelligent computing has numerous instances coordinating multiple satellite, gateway, ground, and IoT device nodes to better match fluctuating user demand with network connectivity resources while preserving speed, accuracy, and performance (including by empowering nodes with proportional fluctuating capacities for data collection, processing, analytics, and functionality). Rather than having to "wait" for human operators to make slow, manual management decisions in scalability and resource allocation, such AI-enabled ground and space connectivity brings IT architectures into a new era as human intelligence is embedded into such computer systems and networks. They are thus able to "think" for themselves to achieve the objectives defined by the human operators (including by coordination across diverse stakeholders in the digital ecosystem). The net result of such collaborative and adaptive advances produces the emerging paradigm of "collective [adaptive] network intelligence" to reduce connectivity disparities, concurrently with improved system-wide technical efficiency gains (better-facilitating force multiplying economies of scale).

Essentially, as more people are plugged into the digital ecosystem (enriched by edge computing and extended by NTNs), its constitutive systems (including healthcare systems and their telehealth providers) work better, faster, and cheaper by sharing resources (and the AI-driven embedded

intelligence in such systems which get "smarter" with each new piece of data) (Saad et al., 2019). Much of the late 2010 and early 2020 surge of telehealth innovation was primarily integrating connectivity with digital infrastructure (particularly remote devices) to allow it to be more accessible to the larger digital health ecosystem (Thompson, 2020). The next innovation step increasingly appears to be AI empowering these networks to have such embedded intelligence, expanding prediction-based healthcare pathways and lower-skilled labor to manage the lower cost, and more remote sensing hardware with digital (and particularly telehealth) health care. Such efficiency gains with AI and the related economies of scale therefore can help mobilize healthcare systems' telehealth networks to sufficiently boost affordability and utility for users (by content, services, and thus user readiness) to achieve critical mass connecting to the infrastructure, and so bring to fruition what the GSMA defines as the "key enablers" of internet adoption.

5.6 Al-enabled telehealth uses cases expanding healthcare systems' borders

5.6.1 Value-based strategic expansion

The strategic telehealth expansion of healthcare systems particularly following the emergence of COVID-19 has particularly focused on its advantages of increased access, convenience, and equity (Bestsennyy et al., 2021). Despite the growing incidence and toll that psychiatric illnesses have on individuals and societies for instance, 56% and 70% of U.S. counties lack adult and child psychiatrists, respectively, while rural versus urban communities bear a disproportionate burden of adverse health outcomes including COVID-19 death rates. The increased acquisitions, vending, and rollout of healthcare systems of telehealth companies, vendor services, and internal capacities are being used to increase the breadth and depth of systems' healthcare delivery (particularly behavioral health and specialty care for underserved communities). Greater interest among payors and employers continues to mount for telehealth improving healthcare access (by systems improving availability of more affordable care of acute and chronic conditions including through innovative hybrid remote monitoring and therapeutics with in-home and inclinic visits, built around virtual check-ins, while reducing preventable ED visits and time to effective treatment). Finally, equity concurrently rises with the above trends as the disproportionate burden on societally disadvantaged communities from chronic conditions and delayed recovery from postacute care conditions can be improved as access to convenient and affordable care rises.

Support for improved value-based strategy including from government and regulatory bodies enhances the above telehealth expansion of healthcare systems by recognizing the worsening disparities that can result from value-based healthcare (Gondi et al., 2022). Take, for instance, the transition from regressive to progressive value-based payment as a countermeasure to this unintended but widespread trend. Despite government incentivization that has spurred payor pressure for healthcare systems (while influencing regulatory measures) to provide such care since the 2010s, there is widespread critique that even the largest and longest-lasting value-based payment models have fallen short demonstrating any significant (let alone sustained) quality improvement or healthcare expenditures. The U.S. Medicare Merit-Based Incentive Payment System (MIPS) and all three of its hospital value-based programs may have actually worsened disparities by shifting resources away from safety net clinics and hospitals caring for a greater proportion of poor and minority patients (by penalizing them for such patients' worse outcomes compared to richer and thus often healthier patients who have better outcomes often even without significant healthcare system interventions) (Johnston et al., 2020; Aggarwal et al., 2021). Medicare's new ACO Realizing Equity, Access, and Community Health (ACO REACH) model addresses such trends by modifying its design of value-based healthcare to include equity: its health equity benchmark adjustment (paying ACOs more if they care for more societally disadvantaged populations), health equity plan requirement (mandating ACOs identify disparities and countermeasures in their communities), and equity-related data reporting (requiring ACOs to track demographic and social determinants of health for their communities to inform better nationally, regionally, and locally coordinated disparity reduction initiatives) are three of its key pillars in this direction (Gondi et al., 2022).

As safety net healthcare systems serving a greater percentage of socially disadvantaged communities (and thus traditionally allowing them a lower operating margin and compensation for care) places increased political economic pressure on systems to expand their telehealth services, not just to survive but also to adhere to increasingly equity-conscious regulations and payment incentives (as significantly more affordable options than building new facilities or recruiting more providers with less capital and recruitment power). Such pressures translate into greater interest for healthcare systems to particularly seek out and adopt AI-enabled telehealth services and their larger IT architecture given the greater data-driven imperatives (to not only identify but address inequities, value-based healthcare incentives, and competition from neighboring systems increasingly moving in such a direction). Systems are thus increasingly turning to service-orientated architecture for their IT architecture (emphasizing its constitutive telehealth infrastructure) to bypass the traditional telehealth challenges to interoperability (across telehealth, EHR, and communication networks and stakeholders as part of the telehealth pipeline of data communication), integration (linking the above data once interoperability is achieved), and vendor lock-in (as there are no dominant end-to-end telehealth vendors yet, thus requiring healthcare systems to often rely on diverse vendors not all who have interoperability if vendors even

permit nonexclusive partnerships in the first place) (Shaikh et al., 2008). Edgecloud computing advances in the telehealth and larger digital health ecosystem are increasingly offering promising solutions by focusing on telehealth integration as central to healthcare system design, strategy, and operations (depending on Big Data to process the flood of data and AI to process, predict, and augment decision-making based on it).

5.6.2 System design with AI-enabled and geospatial informed telehealth

The Association of American Medical Colleges (AAMC) represents and regulates 171 U.S. and Canadian medical schools along with over 400 academic healthcare systems, exercising significant global influence by defining mandatory standards of school curriculum, accreditation, and associated system operations (AAMC, 2022). Its 2021 report on telehealth focused on integration in the various system domains to achieve "successful telehealth programs," encompassing mission (honoring academic and community missions to advance equity via research and education continually improving clinical care), strategy (with leadership and cultural buy-in), clinical (with existing healthcare delivery sites, services, accountability structures, and performance measures), IT (with digital front door into the system and curating user experiences throughout virtual and physical interaction with the system, backed by user and provider IT support), operational (optimizing and scaling within existing scheduling, billing, compliance, licensing, and credentialing processes), and financial (aligning incentives and optimizing reimbursements complementary to systems' portfolio of income generating activities) (AAMC, 2021).

Integration-focused, AI-enabled telehealth applications are therefore proliferating with innovative development in their structure, embeddedness, and effectiveness. Telehealth organizational frameworks include decentralized, hub-and-spoke (often single layer of spokes branching from a hub i.e., hospital), dandelion (subspokes branching from spokes which branch from a hub), and holistic (with portals operating without a hierarchy but aligned with a system's strategic and operational framework) (Bhaskar et al., 2020). Within such frameworks, AI-enabled telehealth developments have been rolled out to improve existing system products and services. ML telehealth analytics has sought to bypass certain limitations of traditional statistical analytics to identify more real-time and generalizable models that better eliminate redundant features, identify combinations of synergistic features, and constrain operations within cost-efficient parameters to accelerate the accurate and efficient diagnostic processes (combining genetic, clinical, blood, and imaging data as needed) (Pacis et al., 2018; Ahuja, 2019). Often the most successful AI and telehealth applications feature a "human in the loop" design with AI augmentation of human providers, including reducing the error rate of diagnosing cancerous lymph nodes, rather than relying on AI or providers exclusively (Jarrahi, 2018). Diagnosis, monitoring, and treatment may be boosted by such telehealth solutions boosting healthcare resiliency, especially during particularly vulnerable periods such as wars and pandemics by helping preserve patient access to providers (Hollander and Carr, 2020).

Such resiliency can further be boosted by telehealth facilitating healthcare systems better integrating their clinical and population health operations, as with geospatial AI (GeoAI) applications like Google Flu Trends combining the National Climate Data Center's Big (spatial) Data and DL recurrent neural networks and even bioinformatics' gene modulation (altering their expression) and docking (studying and modifying molecular interaction) to predict infectious disease outbreaks and their evolutions capable of becoming future pandemics (Venna et al., 2018; Ahmed and Abouzid, 2021). Similarly, ANNs applied to CDC influenza-like datasets and geotagged Twitter tweets produced real-time infectious disease spread, while ML applied to an integrated ecosystem dataset (of influenza-related Google Patterns, past flu trends, and cloud-based EHRs) predicted annual influenza spatiotemporal burden of disease (Hu et al., 2018; Lu et al., 2019). An emblematic case use of value-add and AI-enabled telehealth capabilities allowing streamlined integration with healthcare systems (plugging the gaps in underperformance particularly in disparities) is that of Geospatial Analytical Research Knowledgebase (Geo-ARK), a web-based geospatial Big Data ecosystem (Haithcoat, 2022). Geo-ARK applied to a North Carolina telehealth program precisely demonstrated how poor and rural communities had worse health disparities, lower traditional healthcare system access, and higher telehealth demand and subsequent utilization than their rich and urban counterparts (based on multifaceted and multisource census, zip code, social determinants of health, health, and disparity datasets). Such analytics do not simply say there is a problem—it quantifies and maps it to provide actionable results for healthcare systems to better distribute telehealth services, extend their borders to underserved communities, and improve their performance for their existing patients (where traditional physical services may be falling short of effectiveness, efficiency, and equity targets).

5.6.3 Telehealth implications for patient safety

In this chapter, we have considered how AI-enabled telehealth can help accelerate the clinical and data integration of healthcare systems to improve clinical effectiveness, cost-efficiency, and societal equity by helping identify and address unmet healthcare needs, particularly for traditionally underserved populations including the poor, minority, and rural populations (who historically have faced steeper barriers to access to affordable, convenient, and effective healthcare). In the clinical conceptual model of AI Health and the future's emerging model of healthcare systems, telehealth as the tendons can

connect the PubHealth "skeleton" of systems with the muscle operations of increasingly PrMed-informed and even-based clinical operations. We are not yet at the point in telehealth hospitals were provider labor and resource shortages can be potentially ameliorated by a hybrid in-person and virtual or telehealth capacities (i.e., where robotics and allied healthcare professionals extend the reach and efficiency of physicians and nurses through their telehealth augmented daily operations, while syncing similar operations with home and clinic-based monitoring and care). Yet there are a growing number of discrete problem-focused applications we have analyzed in this chapter in which advances in the AI-accelerated digital health ecosystem and its constitutive digital health infrastructure are "filling out" gaps in healthcare systems. We have additionally considered how telehealth accordingly may help reduce the digital divide that can otherwise inflict particularly high negative consequences in healthcare outcomes, while considering how connectivity, infrastructure, and service fruition developments may address such challenges. So as more gaps are being plugged within healthcare system, we can now turn our attention to patient safety within healthcare systems, including how AI-powered advances may boost a central pillar of system operations—seeking to do no harm while delivering needed value-based healthcare equitably and affordably.

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7842132/

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Chapter 6

AI + patient safety: adaptive, embedded, intelligent

6.1 Patient safety: debates and definitions

6.1.1 Overview of scope and aims

Modern healthcare is inherently risky. As the chapter on its overview discussed, much of healthcare is focused not on prevention (that is generally safer and optimizes health) but on medical care (which is generally more dangerous and mitigates diseases). Accordingly, the personal risk of adverse effects from underlying diseases and disabilities is compounded by the system risk of delivering complex medical care (that typically requires a probabilistic approach seeking to match correct treatments with the most likely diagnoses to hopefully generate more benefit than harm, with such predictions and attempts may ultimately be ultimately incorrect and unsuccessful, amid dynamic disease courses which can often unexpectedly change or fail to respond to treatment due to unforeseen factors). The safest patient care (from a strict statistical standpoint) therefore may be the absence of any patient care. But patients globally still generally accept some level of risk and so opt for healthcare for treatment, prevention, and rehabilitation, necessitating mechanisms and approaches to sufficiently reduce and keep risk at an acceptable level in the provision of that care. Preventing cerebrovascular disease for instance through healthy nutrition and exercise since childhood is generally safer and more effective than trying to acutely treat medically this disease's acute manifestation as a major stroke. The standard of medical care in most modern healthcare systems is generally speaking to provide an available tissue plasminogen activator (tPA, or its closest alternative) which can quickly and effectively break up the clogged brain vessel and save the patient's functional status and even life (but it may also cause catastrophic bleeding and rapid death). Providers therefore must often act quickly in the acute setting with limited information to integrate biology, statistics, and ethics (amid dynamic regulations, policies, and laws) to provide the most likely net beneficial and acceptable treatment for a patient. Incomplete information and unavoidable cognitive and process errors can undermine systems' capacities to accurately

and promptly personalize the probability of successful treatment (if such statistical data on the likelihood are even available and applicable for a patient), while providers must rely on complex networks of stakeholders and resources in that care pipeline (with any point able to experience individual failures which can jeopardize the safety of the entire pipeline). It is a convoluted process at best.

The wave of advances in medical diagnostics, technologies, and treatments in the 20th century (and accelerating even further in the 21st including with AI, Big Data, and multi-omics) therefore has brought not only an amazing surge of healthcare effectiveness but also the risk to patient safety. Systematic, multisector, and institutional efforts from local to international levels have therefore also grown during this time period to help improve the chance that such medical advances can occur at a population and patient level without sacrificing safety (which is increasingly recognized globally as a nonnegotiable and necessary pillar of healthcare systems both now and for the future) (WHO, 2019). And as the prior chapters have considered in various dimensions of systems thus far, AI is similarly emerging as a critical means to accelerating patient safety given the explosive growth in healthcare's complexity and AI's capacity to reduce the lag between systems' potential and patients' needs. This chapter will therefore consider historically how the concept of patient safety developed, its early wins and shortcomings, and how AI is helping advance it (while also considering safety challenges from AI itself).

6.1.2 Conceptualizing patient safety

Patient safety sounds like a simple idea but can be notoriously difficult to actually conceptualize, let alone operationalize. Safety can generally be understood as an acceptable level of risk (or threat of harm) (Higgins et al., 2022), with patient safety specifically referring to the accepted degree of proximity to standards of medical care as resources permit. Such standards historically are understood as the accepted range of diagnostics, treatment, and rehabilitation as applicable for particular diseases or disabilities. This range is informed by clinical practice and research, with its boundaries and specific content articulated and formalized by medical experts or thought leaders generally recognized by the medical community as such (i.e., physicians, other health professionals, etc.) as competent to curate and advance medical knowledge (Klein, 2006). This knowledge or understanding of the medical sciences' causal description of disease and health additionally entails the efficient means of achieving the end of the craft of medicine, namely, optimizing the chances of advancing a particular patient toward a more complete state of healthy function of the person at a biological and integrative level (including psychologically, emotionally, and socially). Such defined concepts still necessarily entail a certain ambiguity of the conceptual borders and their

operational implications. As healthcare is inherently a dangerous enterprise (because of the harm posed by diseases and disability, and the complexity of healthcare meant to address them), patients willingly and knowingly engaging healthcare systems at least implicitly expect some degree of safety (and thus accept some degree of risk adjacent to the conceptual borders of safety). Yet where those borders are (defined by experts, enforced by authorities, and accepted by patients) can shift.

Such theoretical challenges therefore fundamentally complicate how measures and interventions are designed and deployed to improve safety, how changes if any are quantified, and ultimately how they translate into relevant and meaningful clinical outcomes. Often safety interventions because of time and budgetary constraints have to rely on intermediate markers like the percentage of patient encounters by providers appropriately using isolation precautions (like masks and gowns for providers to be used around patients with particular infectious diseases) which may demonstrate a change in such measures. Though such measures often fail to confirm such changes actually produce meaningful overall clinical outcomes (like the reduced length of stay from infection-related complications, QUALYs, and mortality).

Further at the system level, patient safety has a forward-facing and backward-facing dimension, respectively one that characterizes healthcare system approaches to sufficiently reduce and prevent risk for patient's healthcare delivery while reducing and preventing barriers for healthcare providers to deliver that care. Given the increasing technical and operational complexity of healthcare, systems' services and products (from prevention to diagnostics to treatment to rehabilitation) typically have such a technical breadth and depth that they involve many steps, parts, and stakeholders to administer collaboratively (with each additional unit of the above increasing the complexity of the delivery of care, and the possibility of things going wrong, which can in turn contribute to adverse or unintended consequences for patients and the providers of such care). Patients can get better faster from acute illnesses with more sophisticated treatment, but they can also get worse faster particularly if the treatment is wrong (with a speed and severity that is difficult if at all possible to reverse). Physicians can provide state-of-the-art procedures with unprecedented effectiveness, but they also expose themselves to increasingly costly and even career-ending medical liability incidents even with adverse events that could not have been reasonably prevented (particularly if there is insufficient institutional support staff, mechanisms, and policies in place to prevent and mitigate adverse outcomes, and providers' excessive vulnerability and exposure to lawsuits for them). A pediatrician can perform a well-child check-up for a 12-year-old little girl with minimal required resources: she can typically confirm with a few questions and physical exam techniques that the child is growing as expected and is free of any clear diseases, disabilities, or developmental delays. But if that child, i.e., has a prior diagnosis of sickle cell disease, and at that visit exhibits quickly

6.1.3 WHO's patient safety framework

How can healthcare systems create and nourish sufficient safety measures to keep pace with the growing complexity of modern healthcare? Toward this answer, the WHO definition of "patient safety" conceptualizes it as a "health care discipline" (which developed following the "evolving complexity" and subsequent "patient harm" in modern healthcare systems) meant to ultimately "prevent and reduce risks, errors and harm" to patients in healthcare delivery (WHO, 2019). The WHO elaborates on this conception by re-emphasizing the three pillars of optimal healthcare delivery include not just effectiveness and patient-centeredness but also safety. According to this understanding, the core traits of safe care include it being efficient, integrated, equitable, and timely. The main operational means for achieving these traits include data-driven strategies enabling sufficiently clear policy, leadership support, trained healthcare professionals, and patient participation. According to the WHO, this safety conception rests on a foundation of "continuous improvement based on learning from errors and adverse events." As first introduced in the earlier healthcare overview chapter, this framework emerged from the seminal U.S. Institute of Medicine's 1999 report, To Err is Human, which is widely credited as birthing not only patient safety as a discipline but also healthcare quality (Kohn et al., 2000; Schiff and Shojania, 2022). Their 2001 follow-up report, Crossing the Quality Chasm, conceptualizing safety's role within quality was largely endorsed and adapted by the WHO in the ensuing decades (IOM, 2001). The 2002 World Health Assembly resolution on patient safety (framing

it as an integral part of global quality of care) helped spotlight safety and adverse events (WHA, 2019). But despite over 2 decades of sustained and intense international and institutional focus and work on safety, there is widespread criticism ranging from the WHO to seminal contemporary leaders in patient safety that the discipline of patient safety is falling short of its initial noble vision, leaving patients still regularly and widely harmed as they seek help (WHO, 2019; Schiff and Shojania, 2022; Liang et al., 2019).

6.2 Patient safety: development versus defeat

6.2.1 Is (equitable) patient safety failing?

Since the emergence of patient safety as a discipline with sustained international efforts to advance it throughout systems and societies, there have been large, high-profile studies demonstrating improvements in adverse inpatient event rates, with broader improvements from 2011 to 2019 compared to 2005-11 (Eldridge et al., 2022; Wang et al., 2014). But ultimately, there have been no clear, consistent, sustained, widespread, and substantive improvements in patient safety—there has not even been a peer-reviewed study demonstrating clear and longitudinal reduction at the region-level in adverse events (Schiff and Shojania, 2022). Even the above prominent studies (along with related and smaller research examples) indicate that safety measures may be associated with mild improvements at best of adverse event rates (typically 3%-7% relative risk reduction for various admission diagnoses), are shortlived, have unclear if any contribution to overall mortality and quality of life, and are typically isolated to acute care in developed nations predominantly in North America and Europe and mostly only for the transient funding period (after which time provider and system achievement of such measures fall often profoundly and promptly once the financial incentives and management pressures are removed) (Macklin-Doherty, 2018; Meier et al., 2021). The 2010 U.S. DHH report documented how nearly 1 of every 3 Medicareinsured patients suffered inpatient harm, of which nearly half could have been prevented (i.e., missed antibiotics contributing to mortality from uncontrolled infection) (Levinson, 2010). Those sobering statistics were nearly unchanged in 2020 despite billions of dollars and a decade of safety interventions nationally (Grim, 2022).

Such results appear worse globally, especially in lower-income states and healthcare systems (with less dedicated funding, personnel, and resources to focus on patient safety). Unsafe healthcare delivery currently is among the top 10 causes of death, with poorer nations bearing suffering significantly worse disparities in unsafe care compared to their richer counterparts (Jha, 2018). Up to two of every three adverse events (with a comparable rate for the years lost to death and disability-adjusted life years [DALYs]) happen in low- and middle-income countries. Inpatient adverse events appear to account for 15% of all total hospital expenditures in principally high-income nations, representing not only direct cost addressing the negative effects of the event but also the indirect or opportunity cost of having to redirect hospital activities away from more profit-generating ones (Slawomirski et al., 2018). Such expenditures are projected to therefore account for at least 30% of low- and middle-income nations (with less resources to reduce risk and respond to adverse events), though the data for such is notably limited, as is patient safety monitoring, research, and event reporting.

Has anything shown at least some signs of success in patient safety? The discipline of patient safety to its credit has generated a sizable and global movement of eminent (often heavily publicized and many even well-funded) agencies, campaigns, conferences, peer-reviewed journals, trainings, and academic researcher figures. Yet what society has received for its investment is difficult at best to quantify or confirm. Paradigmatic patient safety interventions like medication reconciliation suggest some reduction in medical errors (but not actual harms), surgical and procedural checklists lack sustainable effectiveness in patient safety, computerized decision support systems thus far appear to be more promising than actually effective (with repeated studies pointing to nearly 100% over-ride rate of providers ignoring alerts amid significant omissions in such systems of clinically relevant errors) (Urbach et al., 2019; Schnipper et al., 2022; Marang-van et al., 2016; Kwan et al., 2020; Shah et al., 2021; Wright et al., 2018; Schiff et al., 2015; Shojania, 2020). Initially promising safety interventions may suggest they will help improve patient outcomes, but they typically ultimately fail to actually do so in rigorous outcome testing (while they generally fail to scale sufficiently even to the healthcare system or region levels) (Shojania and Beyond, 2020; Shojania and Thomas, 2013).

Is there an even deeper problem with patient safety as a concept or in practice? Patient safety as a paradigm has historically focused on a systemsbased approach to identify drivers and countermeasures to prevent and mitigate adverse patient events, yet the majority of actual interventions are individual behavior-focused (including mandatory education, alarms, and policies for providers) (Schiff and Shojania, 2022). There is therefore growing interest and investment within the patient safety movement in systems-based approaches like design thinking, human factor engineering, improved collaboration (of diverse stakeholders in healthcare delivery including pharmacists and allied health professionals), and more adaptive system responses (including provider staffing and resource to patient ratios) (Kellogg et al., 2017; Reed and Card, 2016; Neily et al., 2010; Shojania et al., 2020; Leape et al., 1999; Kucukarslan et al., 2003). The general global consensus among systems, policymakers, and patient safety researchers appears largely to indicate that the theoretical framework of patient safety noted above is sound, but it may be incomplete to allow sufficient operationalization (to demonstrate real, lasting, and fair wins for patients and populations the world over). The

central theme therefore of the current patient safety literature regarding its future direction appears to assert that interventions need to be designed, implemented, monitored, and adapted with greater complexity, collaboration, speed, scale, and efficiency. Yet none of this can be practically achieved without Big Data to orchestrate the data flows and AI to make sense of it to enable prompt and increasingly accurate decisions. So if patient safety needs to become more complete and complex in its approach, can AI make it smart enough to get the job done?

6.2.2 Al-enabled patient safety: definitions to development to deliverables?

Invoking the WHO's definition of patient safety, denoted by its prioritization of "continuous improvement based on learning from errors and adverse events," AI seems promisingly positioned to fill the efficiency gap from contemporary healthcare systems' hazardous present and its potential safer future. As the prior chapters have explored, AI is fundamentally the technological capacity to expand our computational effectiveness (to gather, process, and understand data to better predict, act, and adapt based on subsequent data). It is fundamentally about learning better and faster. If the patient safety community, while acknowledging its important advances in the 21st century, note its persistent shortcomings in getting systems to the point where patient safety is standard for all, does this mean AI-enabled patient safety is the next needed step forward? As the prior chapter's clinical conception of AI Health detailed, AI-enabled patient safety may be able to serve as the "immune system" for the healthcare systems. It may sufficiently reduce in systems both internal and external risks (including not only excess medical errors concurrent with insufficient institutional safety mechanisms, but also larger societal threats like supply chain shocks, infectious disease spread, poverty, climate change, and geopolitical conflicts undermining system capacities to respond to patient needs). Our biological immune system utilizes both positive and negative feedback loops. It enhances the actions of its constitutive parts like B lymphocytes to sufficiently fight pathogens (i.e., immunity), while also downregulating the system's response to avoid collateral damage from excessive response (i.e., tolerance). Can AI in systems supercharge both loops?

To see where AI may plug the gaps in current underperforming (or potentially even stalled) patient safety efforts, it may be helpful to consider the prioritized areas identified by the 2018 report of inpatient harm events by the U.S. Department of Justice Office of the Inspector General (OIG) (Grim, 2022). To optimize patient safety, it made three recommendations to CMS: (a) publish guidance for surveyors to track hospitals' compliance with mandatory monitoring for patient harm; (b) expand its catalog of hospitalacquired conditions (HACs) to include costly, preventable, and common harm events; and (c) test and scale as possible patient safety measures for

healthcare delivery and payment models. The OIG additionally made four recommendations to the AHRQ: (a) deploy a national education program for healthcare systems and providers on standards of care (i.e., best practices or national clinical practice guidelines); (b) improve utilization of the Quality and Safety Review System, which may include automatic data capture; (c) coordinate Quality Strategic Plans personalized; and (d) sustain current development of novel harm reduction strategies. Common to these seven priorities, which exercise outsized influence on the U.S. healthcare sector (and thus the global healthcare sector), is enhanced data collection, analysis, and data-informed decisions, with an emphasis on precise and rapid development, deployment, and optimization of safety interventions for local use (fueling additional interest in AI-enabled Big Data to address these domains for which they are uniquely designed and suited).

Following this report, a 2021 research team from IBM Watson Health provided a review of current AI efforts to advance such patient safety approaches, proposing particularly their projection of AI achieving "the greatest impact" where prior and current measures have practically failed and prove insufficient for the related data complexity realities (Bates et al., 2021). This complexity encompasses the collection, (interoperable) integration, and analysis of historically underutilized or untouched (often unstructured) data, especially when accurate predictions require such data (including diagnostic errors, clinical deterioration, and adverse drug events). The 392 reviewed studies seeking to address such safety barriers were grouped according to the eight common patient safety domains (focused on specific major adverse events), in addition to the three noted above: HAIs, surgical complications, falls, pressure ulcers, and venous thromboembolism. The most prevalent novel data type collected was done using such remote sensors as vital sign monitors, computer vision, wearables, and pressure sensors. Therefore, the AI-enabled patient safety literature up to this point generally has focused on improving data flow and its related decisions in isolated clinical situations. Little if any of such research has focused on lower-income communities and nations, let alone scalable and adaptable measures embedded within systems. So to understand such AI measures' increasing system applications and their equity dimension, let us dive deeper into particular leading case uses and how they are being adapted and scaled for system, region, national, and even global needs (from strategy to practical use cases to system-embedded operational advances).

6.3 Human-centered, standardized, Al-enabled patient safety

6.3.1 Patient safety as human-centered design thinking

Patient safety can be understood from a care delivery standpoint as the minimum accepted standard or floor for healthcare systems. The maximum or

aspirational ceiling is the value at which systems deliver desired quality healthcare products and services that are effective, efficient, and fair. Yes, healthcare should "work" to make us better, but before doing so it must at least not do harm to us en route to this desired destination. These two delivery pillars frame the desired healthcare system of the future, while anchoring internationally shared system demands from patient populations in the design or blueprint that gives rise to actual systems in practice. Value-based healthcare cannot occur without safety, nor does safety just happen—it is the cumulative product of a myriad of deliberate decisions by providers, professionals, leaders, and stakeholders in healthcare systems and as such is a necessary component of systems' design. Patient safety (and AI for that matter) require such 'design thinking' so they can be effectively used as means to the end of value-based healthcare to advance patients' and populations' health as best as possible. The American political scientist, AI pioneer, and Nobel Laureate, Hebert Simon, is credited with creating the seminal principles later recognized formally as design thinking which describes essentially deliberate learning with a particular organizational application (You and Hands, 2019; Huppatz, 2015).

Simon proposed design thinking as a systematic problem-solving approach that seeks to identify, test, and ultimately optimize the actions required to bridge a current situation to a more preferred situation. His RAND contribution to digital computing provided seminal development of AI in the 1950–70s by describing human intelligence (in a simplified manner) as logical rules which could be simulated by computers and ultimately applied to solving complex situations exceeding individual human cognitive capacities. Humans in this account therefore have "bounded rationality" according to Simon as we can only take in a small amount of data from objective reality and utilize such data to a small degree to formulate problems (typically how to identify the means or actions to achieve an end) and iteratively test possible solutions until a satisfactory (not optimal) choice of means can be made. As our decisionmaking capacities are bounded by our inherent cognitive limitations (dwarfed by the larger scale of such problems), AI as computing power is thus meant to augment our capabilities to make increasingly satisfactory decisions to reach our ends with increasing effectiveness and efficiency (while bounding computing power by human decision-makers' ultimate role of defining goals and framing choices).

Simon's contemporary, the German design theorist, Horst Rittel, formulated such real-world problems that exceed human capacities as complex "wicked problems" (characterized by often changing, contradictory, incomplete, and interdisciplinary data) that challenge our ability to solve them consistently and successfully (Rittel and Webber, 1973). As Simon developed AI as a paradigm shift in new solutions to such problems, Rittel developed a complementary conceptual framework later termed "human-centered design" as a problem-solving approach that is adaptable, collaborative, and grounded in the complexities of our behavior. As Simon and Rittel would develop the technical aspects of these methodology innovations, the American management consulting firm, IDEO, popularized and practically accelerated their operationalization by describing design thinking ultimately as "humancentered design" that seeks to understand an audience's needs and personalize solutions in three phases: inspiration (empathetically learning what people want), ideation (formulate a wide range of solutions that are ultimately refined to the most promising), and implementation (iteratively running through the above process until a product-market fit is successfully achieved) (Landry, 2020). Human-centered design therefore seeks to radically enhance diverse sectors' decision-making processes by leveraging diverse team's creativity and commitment to accurately frame problems, fail quickly, and achieve novel solutions. The unique approach and consistently successful track record of human-centered design support the building optimism that it may be the most significant advancement in organizational theory in the 21st century, and that when paired with AI as potentially the most significant technological advancement (by range and efficiency) occurring in the Fourth Industrial Revolution may ultimately produce solutions to our biggest unsolved problems.

In the healthcare sector, this includes value-based healthcare that is effective, affordable, and fair (which is thus required for the rest of the world's economic sectors and ultimately our world to function). So how can humancentered design be deployed to AI-enabled patient safety to get us firmly on the road to value-based healthcare? Philips argues that AI can accelerate the capacities of healthcare systems to deliver the care patients need (beginning with it being safe), but it specifically requires human-centered design to do so (Carney, 2021). This can empower systems to deploy AI first and foremost to prioritize and solve real-world problems where existing approaches fail, rather than to use AI as a marketing gimmick or clinically irrelevant tool that therefore typically underperforms on its stated objectives. By more precisely matching the need with the solution, human-centered AI can from design to deployment to refinement better build trust and deliver on demands for patients, providers, and payors. Such theoretical advantages are nowhere more critical than patient safety, arguably the most important and urgent area for healthcare AI. Once AI can help make systems sufficiently safe, they can move on to optimizing their value-based performance (which requires safety as its first necessary deliverable). If such AI-enabled safety is embedded into systems by their organizational DNA (or their design), then it can mature at least in theory into value-based systems.

6.3.2 Standardizing Al-enabled patient safety as system strategy

A joint 2020 report by the EU's European Institute of Innovation and Technology (EIT) Health program and McKinsey invoke distinctive elements of

human-centered design to outline how AI can transform healthcare systems (particularly with safety): delivering healthcare that is more responsive to the clinical effectiveness, cost-efficiency, societal equity, and personal preference demands of patients, along with providers' person-centered and risk reduction (burnout and excessive liability) demands (Spatharou et al., 2020). The main operational means for systems to achieve these strategic goals are the simplification and standardization in AI-augmented best practice domains related to clinical (evidence-based and expertise-confirmed standards of care), technical (data collection, processing, storing, sharing, and analyzing), financing (reimbursements for R&D and augmented care), and equity (international collaborative centers for excellence and research and teaching sharing the knowledge and resources for best practices). Patient safety in this conception of AI-enabled healthcare delivery is principally that of restriction and repetition. It helps define the limits to which healthcare products and services (and the AI that supports their delivery) are permitted to operate in the pursuit of effectiveness and efficiency, while also emphasizing the repetition of embedded and operationalized best practices such that safe care moves from deliberate design and deployment to routine reflex and real-time revisions.

A widely used and fundamentally influential approach to such simplification and standardization of AI-enabled best practices includes regulation focusing on safety assurance frameworks minimizing conflicting, overlapping, and excessive safety regulations that hinder needed system operations, growth, and optimization. The 2021 comprehensive global report of contemporary standards in AI healthcare was detailed by the British Standards Institution (BSI), the UK's Royal Charter-backed national standards body, the oldest national standards body, and a world leader (by size and influence) in professional certification and standardization (including for practice, guidelines, and product specifications), serving over 84,000 clients in 193 countries (BSI, 2022). BSI detailed 236 contemporary standards spanning six focus areas (with the largest being "Health IT" at 103 standards) and three assurance categories (ranging from more suitable for assurance particularly already operational standards i.e., in medical device regulation to "less mature best practices" such as general use of AI). Only 6% of standards were classified as "assurance requirements," leaving 13% being "supporting" and thus 82% being "informative" (p. 33). Globally, there is only one standard specific to AI (and particularly ML) for the healthcare sector, and it is only in development rather than not actual use. The BSI emphasizes the unique challenges to patient safety that include this underdevelopment and ambiguity of such standards amid the diverse authoritative bodies tasked with regulating diverse aspects of safety (from government, professional, and industry bodies). It advocates for "a safety assurance framework for AL and ML in healthcare" therefore to generate specific, reasonable, necessary, consensus, and collaboratively produced and enforced standards. Such a framework can thus empower sufficient assurances for patients and societies that the corporations,

systems, and providers as the stakeholders in their healthcare will reliably meet "regulatory and patient safety obligations" through the instrumental "best practices and guidance" (p. 34). In the meantime, general consensus is that current laws internationally place final accountability on the shoulders of providers (who are largely not knowledgeable about AI best practices let alone their related liability and risks to patient safety), and thus there are an increasing number of systems and parallel AI organizations utilizing a human-centered design approach to build embedded AI healthcare products with "compliance by design" (to foresee and mitigate risks within the current regulatory landscape) (Spatharou et al., 2020).

6.4 Al-enabled patient safety use cases: drug safety, clinical reports, and alarms

6.4.1 Al pivot

We have so far considered how the lack of sustained progress in patient safety in the 21st century thus far has not only galvanized such top-down organizational innovations as human-centered design and embedded safety standards as noted above, but they have also facilitated the increasingly prevalent prioritization of AI-augmented bottom-up technological innovations being tested and scaled in healthcare systems to hopefully succeed where traditional approaches have fallen short (Liang et al., 2019). Most people do not consider flying to be an excessively dangerous endeavor-safety comes standard largely when you get onto a plane. Similarly, as multiple industries have paired time-tested intense safety engineering with emerging AI applications (particularly ML) to streamline and optimize workflows and protocols amid complexity and risk, the healthcare sector is witnessing increased safety use cases of AI particularly in improving patient risk stratification and mitigation, acute-chronic care continuum, medication safety and adherence, PrMed, and experience (Symplr, 2021). Accordingly, a 2020 systematic review of the preceding decade demonstrated growing AI-enabled patient safety measures with empirical testing of effectiveness (Choudhury and Asan, 2020). The primary safety subcategories of AI applications from largest to smallest included drug safety (n = 23 studies), clinical reports (mostly using support vector machine [SVM] models; n = 21), and clinical alarms (most commonly using decision tree models; n = 9). This growing trend of empirically tested AI safety use cases demonstrated improvements in medication management, patient stratification, and error detection—and notably unlike the above-noted self-critique by the patient safety community, such cases have demonstrated sustained and consistent improvements in ultimate patient outcomes including morbidity and cost (which we will explore shortly). Yet these studies largely failed to show any AI reporting or performance standards which thus challenges their scale, personalization, and diffusion of best practices in their

systems and across others to fit their respective needs and resources. So let us explore in more depth the particular subcategories of AI use cases to better understand their potential and limitations especially for drug safety (Hammann et al., 2010), clinical reports (Klock et al., 2019), and alarms (Hu et al., 2016). We will focus on these top-performing studies by accuracy (the number of correctly predicted samples divided by the total number of samples), as it is one of the most utilized, accepted, and intuitive algorithm metrics (particularly for non-technical audiences) evaluating different AI models especially in classification (Zvornicanin, 2021; Florkowski, 2008). Where accuracy is not available, we will utilize the receiver operating curve area under the curve (ROCAUC), which similarly enjoys widespread use and acceptance as a popular metric. But unlike accuracy, it has the advantage of measuring accuracy along with its probability. It graphically represents on its x-axis the false positive rate or 1 minus specificity (false [or incorrectly classified as] positives divided by the sum of true [or correctly classified as] negatives and false positives) divided by x-axis of the true positive rate or sensitivity (true positives divided by the sum of true positives and false negatives) at different thresholds of probability for model predictions. It should be noted that there is no widespread agreement for the optimal summary metric to compare diverse AI algorithms, and typically there is a wide range of metrics utilized for any given study including, F1 score, etc. But for our illustrative purposes below for a diverse technical and nontechnical audience, we will utilize the above.

6.4.2 Al drug safety

Hammann et al. (2010) utilized decision tree AI algorithms (chi-square automatic interaction detection [CHAID] and classification and regression tree [CART]) on 507 pharmaceuticals from the Swiss drug registry to predict complex end-organ adverse drug reactions (ADRs) according to the drugs' chemical, physical, and structural traits. Accuracies of 90.22%, 89.74%, 88.69%, and 78.94% were, respectively, achieved predicting liver, central nervous system (CNS), renal, and allergic ADRs with these simple AI models using the publicly available dataset to inform drug design (by compound selection and interaction modeling) and postmarketing pharmacovigilance (drug safety monitoring after clinical trials and regulatory approval for market use).

6.4.3 AI clinical reports

Klock et al. (2019) utilized SVMs and RNN algorithms paired with the AHRQ rubric grading the quality of patient fall reporting to better identify root causes of falls (enabling enhanced human-centered design prevention) while reaching accuracies of 0.899 (SVM) and 0.900 (RNN). Notably, this study determined that the majority of such mandatory reports are of low quality, limiting their utility for patient safety improvement despite such reporting being compulsory by healthcare systems for diverse bodies and purposes (ranging from reimbursements to ratings to medical liability to accreditation). Consistent with the 2018 OIG report noted above, the increasing prioritization on improved data collection and reporting (which is unclear how they can be accomplished without AI-enabled Big Data) appears increasingly key in potentially translating the last 20 years of patient safety focus into actual patient safety improvements.

6.4.4 Al alarms

Hu et al. (2016) utilized an ANN on EHR data to demonstrate an AUCROC of 0.880 along with superior performance compared to the VitalPac Early Warning Score (VieWS), one of the most commonly used and best performing early warning systems for inpatient clinical deterioration (defined as cardiac arrest or emergent need for intensive care unit [ICU] transfer). This has an immediate real-world application as it uses EHR data already available to provide clinically relevant, real-time warnings to allow timely treatment changes as needed to mitigate the risk of adverse outcomes.

6.5 Automating Al-enabled patient safety: embedded, ambient, command center, and blockchain intelligence

6.5.1 Integrating scaled AI safety processes in healthcare systems

If AI is to empower patient safety measures to be effective, efficient, fair, sustainable, and scaled throughout systems globally (where pre-AI interventions may have fallen short), it requires successful integration within healthcare systems. We have explored above how such organizational innovations as human-centered and standardized design can assist with this. So the question becomes how this design-accelerated integration can occur particularly with the above AI-enabled safety measures of drug safety, clinical reports, and alarms (in addition to related emerging use cases)? We can now analyze the growing trends of embedded, ambient, and command center technical approaches to advance this project along with the additional element of data security (assisted with blockchain) to facilitate overall patient safety.

6.5.2 Embedded, ambient, and command center safety intelligence

We have explored previous innovations generally embedding AI solutions in healthcare systems to minimize disruption to existing workflows (and data architecture) to thus maximize force multiplying productivity boosts as the physical system is further digitized (with an increasingly sophisticated data architecture to match the needed Big Data and AI capacities required for

systems' needs). Particular patient safety interventions guided by (a) embedded (with EHR-based automated audits and drug safety), (b) ambient, and (c) command center intelligence are increasingly promising (and to some degree even consistently demonstrated) AI measures sustainably improving patient safety to scale.

(a) Novel safety embedded measures with the "medical algorithmic audit framework" and EHR-based medication reconciliation are gaining traction for system use by introducing innovations technically and organizationally (through an embedded intelligence paradigm generating ongoing adaptive changes to the framework and reconciliation to sustain the safety boosts over time and subsectors within systems). The audit framework was developed by UK, Australian, and U.S. clinicians, computer scientists, and ethicists to address the dual threats of AI deployed in healthcare of precision safety (when AI algorithms developed and validated in datasets that are not representative of the demographics and comorbidities of patients to whom they will be applied) and the parallel issue of technical reliability (when the algorithms fail to adapt to new contexts i.e., new devices and hospitals) (Denniston and Liu, 2022). This framework takes seriously the contemporary technical challenge of scalability (not simply up through a system but even to a system for clinical practice from research practice). Like a resident-physician becoming an attending-physician (moving from residency training to unsupervised medical practice), an AI algorithm can test well in structured studies but ultimately fail in clinical practice to achieve the intended clinical objectives of safe, quality care. The audit therefore integrates clinical and engineering stakeholders to facilitate comprehensive risk assessments of AI in healthcare before and after deployment, including particular requirements to flag AI underperformance in different patient demographics and settings while also mapping the system failures leading to those failures (to prevent future occurrences). This audit framework can act in real time and be scaled across an entire system through its EHR, as evidenced by a recent AIempowered medication reconciliation innovation (SmartSig) in which a U.S healthcare system (WellSpan Health) contracted a private vendor (DrFirst) to utilize its health IT tool for automatically translating a national database of diverse EHR types from diverse systems into the standard nomenclature for WellSpan's Epic EHR (Nelson, 2022). This discrete solution to a discrete problem cut costs while boosting safety for the healthcare system as there was less need for providers to manually contact other pharmacies and systems to confirm and transcribe into Epic a patient's home medications (manual processes more prone to individual random error). SmartSig's algorithm was additionally able to improve performance over time as it became more accurate with more patient data

- (reducing ADR risk), while trimming approximately 40% off the system's medication reconciliation budget and providers' time by 35%.
- (b) In addition to embedded safety intelligence within existing system workflow and data structures to enhance them, ambient safety intelligence is increasingly demonstrating how it can be anchored *onto* existing flows and structures to reduce risk and adverse events. Ambient refers technically to being immersed or surrounded on all sides (such as with ambient light in a bright atrium entrance of a pediatric hospital) or musically as repetitive relaxing melodies (Britannica, 2022). As the introductory AI chapter noted, Mayo Clinic's AI-driven ambient intelligence platform, AWARE, demonstrated how it can be integrated with an existing EHR and ICU workflow to reduce providers' cognitive and medical errors while improving patient outcomes (cutting mortality odds by over half and costs by nearly \$50,000 per hospital stay) by curating the most relevant and urgent clinical data points which otherwise can become overwhelming (Ahmed et al., 2011; Pickering et al., 2015; Olchanski et al., 2017). Yet this ambient approach can occur organizationally not just technically. There is increasingly prominent and promise of integrating patient care and specifically safety measures with the larger healthcare ecosystem to leverage the diverse resources and expertise of stakeholders, as with Mayo's COVID-19 Healthcare Coalition coordinating the inputs of healthcare systems (including America's largest healthcare system [HCA] and Mayo's portfolio of digital health and AI initiatives), academics, private tech industry (including Microsoft, Amazon, Apple, and Google), and health IT vendors (including Epic) (Landi, 2021). The ambient collective intelligence thus responded in the early days to the public health emergency posed by the pandemic to freely share (without intellectual property or legal restrictions) such innovations as early best clinical practices, telehealth strategies, and NLP-informed national pandemic data infrastructure with decision aid dashboards to ultimately boost safety, effectiveness, and equity.
- (c) Ambient intelligence can pool together massive data, resources, and expertise, but it requires central decision-making to translate it into effective outcomes. This is where command center intelligence may become instrumental (McInerney et al., 2022). Air traffic control, nuclear power plants, and other high-reliability organizations (HROs) have multidecade track records of optimizing safety amid organizational complexity and dynamic risks. These HROs from safety critical industries by design operate within organizational structures with related data architectures that optimize situational awareness, resilience, and reliability to continually predict and adapt to changing risks (to ultimately prevent and mitigate adverse events to an acceptably low level and so preserve societal trust in the organizations). Yet healthcare remains an outlier among industries in terms of its comparable complexity and risk but

disproportionately higher adverse events, with a long publication history demonstrating healthcare systems' shortcomings and delays adapting appropriate safety best practices from other economic sectors. The UK's NHS Bradford Royal Infirmary hospital adopted such practices in 2019 with its "Bradford AI" "hospital command center" as an HRO mission control (developed with patient and public involvement and engagement [PPIE]) to optimize patient safety by improving patient flow (decreased delays) and situational awareness (detecting and mitigating threats). The center utilizes the US firm's GE Kryptonite software on "tiles" or display screens to integrate real-time EHR data with automated predictive algorithms to produce adaptive metrics augmenting clinical and organizational decisions. The center serves as an artificial "brain" for the system that like the human body collects, processes, analyzes, and informs decisions. Flow and EHR data quality affect not only patient safety directly (i.e., too many patients admitted too quickly, along with insufficiently clear documentation of relevant clinical problems, can increase the likelihood of medical error). The command center utilizes time series analyses and latent growth modeling to analyze the actual clinical and cost impact of the center compared to a similar hospital (with comparable EHR), but without the center to reduce the result bias of unobserved confounding factors. Additionally, Bradford tracks safety changes with the AHRQ Patient Safety Indictors and the relevant research literature (including mortality, readmission, HAIs, falls, pressure sores, etc.) with complementary costbenefit analyses and diffusion of innovation through an empirically guided implementation framework to facilitate scale across diverse systems (It should be noted the full and longitudinal results of this command center intelligence were not available at the time of this book's composition as enrollment closed August 2022.).

6.5.3 Data security and privacy: blockchain

Central to embedded, ambient, and command center safety intelligence is the technical necessity of sharing secure data across diverse stakeholders in real time. Yet this can undermine patient safety by increasing the challenge of preserving data security. An emerging countermeasure is health blockchain technology already in testing and refinement in systems, particularly in telehealth as introduced in that respective chapter above (Ahmad et al., 2021). The technical aspects of the blockchain (including data and user anonymity, auditability, immutability, reliability, transparency, and decentralization), which facilitate such practical applications, confidentially and securely protect patient-physician remote consultation data, verify remote physician credentials, and monitor health center locations in addition to medication and diagnostic products through supply chains. Blockchain can accomplish the

above with its consensus protocols (including the structure, parameters, and oversight determined in advance by decision-making stakeholders), public-key cryptography (requiring digital signatures for each transaction or encounter prior to their verification and translation into the ledger), "doctor in the loop" design with tamper-proof log data (allowing expert oversight to maintain data integrity and validity), smart contracts (automating operations through self-executing programs defined by the consensus protocols), and distributed data structure (mitigating accidental data loss and cyberattack threats with decentralized blockchain system administration). AI-augmented blockchain is a particularly powerful data security technique that has paired multiaccess edge computing with blockchain smart contracts for diverse healthcare system functions: blockchain-stored EHR (preserving a master copy free from data deletion or modification by network users), real-time patient monitoring, specialty selection (matching patients by symptoms to the appropriate physicians), timestamped medication log, and even cryptocurrency payments.

6.6 Al challenges to patient safety: bias, reproducibility, explainability, effectiveness, and design solutions

6.6.1 Standardizing bias reduction, reproducibility, explainability, and effectiveness

Though this chapter has explored the promise and progress of patient safety by AI, the threats that it poses to safety should also be considered (along with the respective countermeasures of [a] bias reduction, [b] reproducibility, [c] explainability, and [d] effectiveness) (Challen, 2019; Gibney, 2022). Though such challenges are not necessarily exclusive to healthcare or even AI, they can have an outsized influence undermining patient safety in the healthcare sector, already struggling to optimize safety while still being early enough adopters of AI to increase the likelihood of appropriate integration of best AI practices as benchmarks and templates for subsequent iterative improvements.

(a) Bias reduction has been proposed to address the challenge of automation bias common to such contexts as healthcare expert systems, autonomous vehicles, and the aviation industry. Similar to other professionals, clinicians can excessively trust automated expert-generated algorithms or tools (even when they fail) which can influence deskilling (in which skills atrophy from underdevelopment, such as cardiologists losing through underuse the technical skills to manually read echocardiographs and so detect anomalies and inaccuracies from automated AI reads). The flip side of this automation bias can also occur if providers and system leaders may have an excessive distrust of AI algorithms if they witness early case failures of it despite later progress. Bias reduction may address these challenges through ongoing provider education and system support (i.e., AI-

- supported IT and research personnel assisted by continuous algorithm audits noted above).
- (b) Computational reproducibility, related reporting checklists (collaborative and consensus-based), and centers for excellence diffusing AI best practices may address the challenge of AI reproducibility (especially with DL when black box algorithms produce results which cannot be sufficiently clinically assessed by physicians, or their results repeated by independent teams knowledgeable of the full data, code, and condition details). Akin to how the PRISMA criteria seek to facilitate reproducibility and enhance the validity of systematic reviews and meta-analyses by defining a minimum methodological standard for such studies (Page et al., 2021), the above countermeasures are under development to apply such an approach to AI (particularly DL and ML). They seek to address "data leakage" as part of training data (on which an algorithm is trained) "leaks" into the test data which thus ultimately biases the results with artificial overperformance). Without such rigorous standards in analysis and reporting, irreproducible results can undermine patient safety if deployed in clinical practice before their validity threats are sufficiently resolved. Centers for excellence additionally can assist in providing system, professional association, payor, and government-recognized AI best practices including for reproducibility which can help to appropriately match societal trust in algorithm validity with actual performance of the algorithms (which otherwise can be weakened from unwarranted fear of AI being a perpetual and impenetrable black box). Such centers can assist with accurate public and system communication about the parallels of providers' black box clinical reasoning (in which the "gut feeling" or "clinical intuition" of providers about a patient's risks and indicated treatments may often face difficulty supporting with concrete and formal empirical demonstration and justification) and how consistent, reliable, and accurate algorithm performance can be objectively and independently validated and replicated.
- (c) Enhanced model explainability may address safety threats of "distributional shift" and domain bias. This shift commonly refers to ML predictions or outputs that shift often excessively from the patient populations on which the model is deployed or reflects inaccurate patient outcome labeling (as its training data does not accurately represent the data of patients for whom it is being subsequently utilized). Such inappropriate ML "out of sample" application can further increase the likelihood of adverse events by providing inaccurate recommendations for diagnoses and treatments. Shifts can occur for a variety of common reasons (i.e., different patient demographics or longitudinal clinical changes including dynamic disease courses, in addition to fluctuating diagnostic standards and diagnostic test variability). Additionally, domain bias can further threaten patient safety as data engineers because of an understandable lack of sufficient clinical-specific expertise may create algorithms that fail to

appropriately prioritize clinically mandated model facets (like excessively prioritizing sensitivity over specificity [or vice versa] or failing to appropriately consider clinical severity). An ML model compared to a physician may more efficiently classify skin lesions as malignant versus benign, but the fatal clinical consequences for missing aggressive cancer may mandate significant model revision (which clinicians may not know initially to look for as they typically lack deep AI domain-specific expertise to understand how models are generated, tested, validated, and optimized).

(d) Optimal effectiveness may counter the patient safety issues of technicalclinical mismatch bias in which more AI applications can be generated than what is clinically relevant or needed. In the strategic push to more thoroughly integrate AI in healthcare systems, misplaced hype for AI performance may lead to algorithms that can undermine patient safety by inappropriately reducing the role of physicians in care delivery through task automation or augmentation in ways that do not ultimately improve patients' clinical, cost, and equity outcomes including in ways relevant to them. In keeping with the GRADE system introduced to assess the quality of clinical evidence and strength of recommendations for diagnostic tests and protocols (Schünemann et al., 2008), it is challenging to support AI clinical applications that even in their initial design phase lack sufficient theoretical and related empirical justification for their meaningful positive impact on patient-relevant outcomes. This similarly extends to evaluating algorithm performance, as an AUCROC and related analytic metrics alone do not clearly indicate the likelihood of meaningful and measurable clinical success to support advancing the algorithm closer to clinical use and system scale.

6.6.2 Al design solutions in the safe (future) healthcare system

In this chapter, we have considered the growing and deepening society, state, and system prioritization and investment in new approaches to old patient safety challenges, especially with AI-enabled human-centered design thinking with scalable safety intelligence. We are witnessing increased divergent outcomes (including actual improved mortality and cost) with more recent versus earlier interventions particularly as their design with data collection and analytics becomes more complex, comprehensive, and real time (as facilitated by AI). The successful case uses of AI-enabled drug safety, clinical reports, alarms, and blockchain-supported data security may be promising. But there is growing evidence that they require complex adaptive system approaches to help them make reliable, sustained, substantive, and equitable real-world improvements to patient safety (particularly through embedded, ambient, and command center intelligence allowing systems' safety interventions to

adapt to dynamic patient, population, and system needs and resources with accurate, precise, and standardized risk prediction, prevention). If affordable quality health care is the necessary strategic "ceiling" for the emerging model of the future's healthcare systems, patient safety must be the minimum floor framing this "home" for every patient, in which safety is built into the "DNA" of AI-enabled systems in their strategy, structure, workflow, and culture. But to advance toward concrete realization of such a model, we need to next consider the political economic reality that influences, limits, and inspires the system.

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Chapter 7

AI + political economics in healthcare: globalized, digitalized, divided

7.1 Evolutionary biology, digitalization, and globalization of healthcare political economics

7.1.1 Evolutionary biology

Modern health care is by necessity a team sport, one that practically runs on people and cash. Since no one has all the resources to satisfy her/his desires and needs, we need others in a dense, life-long network of mutual interdependencies to realize common and overlapping goods and goals. Complex social groups at the local level like healthcare systems and societal level like nations self-organize (come together, stay together, and fall apart) according to their common beliefs which inform the ends or goals or good they collectively seek and thus the means they take to attempt to reach them (Monlezun, 2022; Costa-Font et al., 2020). The U.S. healthcare system (as the network of its local systems) looks very different for instance compared to the Chinese healthcare system. The difference in beliefs and values between both nations informs a different set of desired ends of systems and thus the means they take to get there. Should a nation have a nationalized or private healthcare system? Universal health coverage (UHC) or leave it to people to obtain their own insurance? Should a nation directly employ and pay its providers on behalf of its citizens, or leave patients to interact directly with the free market to finance their healthcare individually? How much regulation if any should the healthcare sector have? Such questions take on a growing importance given the growing interdependent ideologies and organizations of local systems affecting how they operate (driven by biotechnology, payors, regulators, pharmaceuticals, researchers, supply chains, and next generation societal trends nationalism vs. AI-enabled digitized globalization). If we do not understand the political economic forces that exert significant influence on (and even define operating parameters for) healthcare systems, then any discussion about components of systems like telemedicine or PubHealth is interesting but ultimately ineffective. To understand how to direct systems in a communally desired direction to hopefully a better AI-enabled future, we may need to look back at what brought our current systems to their current challenges (and how to get them past them).

Dating back to at least two million years ago, broad evidence from our earliest ancestors supports how we diverged from other social primates through cultural evolution (predominantly by cooperative competition organizing human societal units hierarchically to more effectively address complexity, resource shortage, and collective security and prosperity) (Boyd and Richerseon, 2009; Sterelny, 2021; Atkinson, 2011; Mozzi et al., 2016). As genetic mutations in our prehistoric frontal lobes gradually facilitated more complex problem-solving and language (particularly with CNTNAP2, ROBO1, ROBO2, KIAA0319, and FOXP2), our forebearers increasingly learned and communicated what they learned to an increasing number of perceived "members" of their social groups to allow collective action or cooperation for shared survival. This cultural adaptation sharpened persistent differences among social groups as they competed for scarce resources. Certain cooperative and competitive "pro-social" behaviors (and their associated genetic and epigenetic variations) became more prevalent and influential as they boosted the chances of survival for such groups better adapted to their environments (who could then pass on such behavioral and genetic adaptations to their children through natural selection and particularly its related "social selection"). These cumulative changes developed to encompass "moral systems" of rewards and punishments (and related individual emotions like shame and empathy) helping prevent and resolve disputes among parties regardless of their powerful differential through sanctions of third parties (where the stronger would not always be able to act toward the weaker however they wished). More socialized humans and human groups were more likely to successfully cooperate and compete and thus survive to reproduce and expand. Division of labor, large-scale conflict, care for the disabled and sick, and complex language increasingly differentiated human versus nonhuman animals. Politics and economics seek to simplify this long, complex picture, and inform how best we should practically arrange our society toward this destination by organizing power and resources in centralized (hierarchical) and decentralized networks as institutions, customs, and norms.

This applies especially and urgently to healthcare systems. A patient who becomes sick with a lung infection requiring oxygen can only receive life-saving care walking into a hospital if the electrical bill of the hospital is paid, there are providers paid to be there to care for the patient with medications and equipment and food and hydration already purchased, and the key system components participate in a complex set of complementary relationships inside and outside the hospital (obtaining and managing human and non-human capital to ultimately deliver care within the larger community amid societal constraints including regulations, laws, and market pressures from

competing healthcare systems). Such financial and governance dimensions of healthcare systems thus largely determine modern systems' design models and management (and those of AI-enabled advances). We considered in the clinical formulation of AI Health how economics are like the GI biological system and politics like the respiratory system of healthcare systems—they require capital to regularly feed their operations and governance to oxygenate them to allow them to continue the functions of the various components and dimensions of the healthcare system. Therefore, the political economics of systems and their AI-enabled versions are critical to understand where healthcare delivery is now and where it likely is going.

7.1.2 Industrialization and digitalization

"Political economics" refers generally to the social science seeking to understand and articulate the parallel relationships of individuals and societies along with markets and the state that organize human communities and their related behaviors (Veseth and Balaam, 2022). Dating back to at least Plato and Aristotle who sought to understand how and why we self-organize to sustain communal and individual life (along with even how we should), political economics developed through the Scholastic tradition with Aquinas until the Western Enlightenment when the Scottish philosopher, Adam Smith, proposed the first comprehensive account of it. At that time, the field and its primary conceptual principles and frameworks were influenced by an individual focus (from the English philosophers, Thomas Hobbes and John Locke), inductive scientific reasoning (from the English philosopher, Francis Bacon), and the practical often pessimistic assumptions about unidealized human nature and interactions (articulated by the Italian politician, Niccolò Machiavelli). A central doctrine or set of related principles running through much of this European-dominated discipline was described by Smith as the "invisible hand." Societal survival requires political stability which requires sufficient economic welfare (as a basic set of accessible goods, services, and opportunities). Yet state policies are generally inferior to self-interested individual actions to advance collectively toward sufficient societal welfare (for a sufficient number of individuals in a society to achieve and maintain stability). Factory workers may freely choose to go to work at a factory making shoes because it generates acceptable wages for them. The factory owner freely chooses to buy and build and sustain such an institution for the profit it generates for her/him amid the risk of failure. And other factories' owners and workers may directly compete with the above to build either higher quality or lower cost products for consumers of those shoes, doing so in a way that indirectly maximizes the chance of the highest value range of shoes for consumers (meaning this "invisible hand" of accumulated self-interested individual actions produce a favorable political economic net benefit for a society, even if individuals do not directly or deliberately will such overall societal

benefit). This account helped elaborate such concepts as a division of labor, specialization, market competition, wealth growth, and societal rules and institutions (meant to facilitate the above).

These seismic societal changes in turn influenced and were influenced by the concurrent development of modern industrial revolutions, as each subsequent phase triggered fundamental political economic revisions and even national revolutions. Expanding on the description in the AI healthcare overview chapter, there have been (a-d) four major industrial revolutions that have largely shaped modern political economics from a technical standpoint (Rodrigue, 2020):

- (a) The First Industrial Revolution in mechanization beginning in the late 1700s organizationally catalyzed industrial cities through steam engine power and mechanical production, ultimately generating the primary technical innovation of substitution (of traditional human or animal labor with mechanical labor).
- (b) The Second Industrial Revolution in mass production beginning in the late 1800s organizationally catalyzed industrial regions through electrical power and division of labor, ultimately generating the primary technical innovation of economies of scale (with growing human and machine specialization among interdependent elements of the industrial pipeline creating cheaper commercial products from raw materials, guided by geographically larger regions linked by such pipelines and parallel electrical telecommunications).
- (c) The Third Industrial Revolution in digitized automation beginning in the later 1900s organizationally catalyzed global production networks through electronic information technologies, ultimately generating the primary technical innovation of lower input costs (with computer then internetaccelerated global logistics connecting cheaper human labor, augmented by automation with richer regions consuming their products).
- (d) The Fourth Industrial Revolution in interconnection and robotization beginning in the early 2000s organizationally catalyzed global value chains through cyber-physical systems, ultimately generating the primary technical innovation of optimized added value (with AI-powered IoT and Big Data accelerating adaptive international production sharing as multinational division of labor, powered by more sophisticated machine replacement for human inputs as resource collection, transformation into intermediate products, and polishing into finished goods and services which are then sourced and distributed according to global and often shifting production-consumption demands). The digitalization driving subsequent global value chains quickened the deepening political economic interconnectedness and interdependencies, not only of states and sectors but also their embedded healthcare systems (as the healthcare overview chapter introduced how accelerated medical technologies and supply chains catalyzed a global awareness of the globalization of health care).

7.1.3 Globalization

As the PubHealth chapter introduced, modern political economics and Pub-Health became increasingly interwoven under the framework of "global public health" by the early 21st century, as articulated in the 2008 UN General Assembly on "Global health and foreign policy" (UN, 2009; UN, 2008). In the tradition of the Western Enlightenment's political economics, the world's nations collectively and explicitly invoked the reality of "their interdependence" to advocate for a global political economics of self-interested activities, which collectively can produce the secondary benefit of achieving the "healthrelated Millennium Development Goals" (but expanding the definition of "self" to the unified, digitally connected, globalized modern world). Such ambitious goals ranged from eliminating extreme poverty to improving maternal and child health to reducing communicable diseases (like HIV/AIDS and malaria), all in an environmentally sustainable manner within a global development partnership. A modern world is a connected world, and an internationally healthier world is an economically more prosperous and thus more politically stable world, so goes the reasoning. So following the U.S.-led political economics expansion of its liberal capitalist democracy model internationally following WWII (sped up after the 1991 fall of the Soviet Union and 2001 entrance of China into the World Trade Organization [WTO]), the explosive growth of digitally accelerated industrialization at scale and international free trade occurred alongside the plummeting of extreme poverty by nearly 60% from 1990 to 2015 (UN, 2015). Under-five child mortality and maternal mortality have been halved during the same time period, while new HIV infections dropped by 40% and the global malaria mortality rate has fallen by 37%. Ozone-depleting substances have been nearly eliminated, while 2.1 billion more people now have access to improved sanitation and 1.9 billion to cleaner piped drinking water. By 2015, mobile-cellular signal expanded to cover 95% of people internationally, internet penetration linked over 3 billion, and official development assistance from developed to developing nations surged 66% to \$135.2 billion. But beginning in 2016, the increasing manifestation of underlying societal fault lines supposedly along nationalist peoples and elitist globalists (signaled by 2016's Brexit vote and Trump's U.S. election to the 2020 Great Lockdown and COVID-19 recession [with Chinese pullback from global trade] to the 2022 Russian imperial invasion of Ukraine) progressively challenged the 21st century's initial optimism of a new age of global political economics and PubHealth, undermining the confidence in revitalized modern healthcare specifically and global society more generally.

7.2 Overview of macro (ideological) and micro (financial) political economics pressuring modern healthcare systems redesign

(a) Primary macro- and (b) micropolitical economic forces continue to shape how systems collaboratively compete externally (seeking to sustain themselves and thus their market niche amid partners and competitors) and operate

internally (governing themselves and their resources). These primary forces framing such practical dimensions of systems can be respectively understood according to the ideological development underlying political economics (in which healthcare systems are embedded) and their financial day-to-day parameters (within which systems function). Such trends are pressuring a redesign of modern healthcare systems to address growing unmet challenges. Before we can go into more depth and focus on how they impact AI-enabled healthcare system developments, let us consider a brief overview of these forces.

7.2.1 Macropolitical economic forces pressuring healthcare system redesign

Regarding the (a) macroforces, the ideological evolution in political economics describes the historical arch from belief systems or ideologies from societies powered by populations then productivity then purpose (Monlezun, 2022; Veseth and Balaam, 2022; Sachs, 1999; Boyd and Richerseon, 2009). Premodern humanity generally organized politically initially as foragers and then later as farmers, as economic productivity was largely determined by the amount of farmland and children a community had. During this time, empires developed around 3200 B.C. in Egypt and progressed as a series of international political economic units often created through military victories or consolidation of power from a central conqueror, were governed from a dominant center and featured peripheries of multiple regions and peoples or nations (or societal groups noted above) (Howe, 2002). While largely dependent economically on agriculture, politics served to defend and expand land and laborers, typically in a life cycle widely experienced by these societal units from regionalization to empire ascension to maturity to overextension to decline and postcollapse legacy (Murrin, 2011; Maier, 2007; Vaughn, 2021). The Persian, Chinese Han, Indian Indus, Mayan, Islamic Umayyad Caliphate, Mongol, Ottoman, Spanish, Russian, British, and American empires demonstrated notable consistency in how the common "moral systems," beliefs, or stories not only constituted a common identity (manifesting as shared ends and means) but also indicated the decline and eventual collapse of such units once this foundation of competitive cooperative structures failed. Overlapping during this political development was the latest economic development from population to productivity ideological evolution which soon thereafter precipitated the final phase focused on purpose. The 16th century Scientific Revolution generated what began in Britain and then transitioned to the US as the ensuing Industrial Revolutions and related philosophical revolution of the Enlightenment, unleashing unprecedented efficient economic productivity supported by the accompanying political values of individual freedom, equality, progress, tolerance, and representative constitutional government. As this productivity became more mechanized and eventually digitized, it became

also more globalized. From the 2008 Global Recession to the 2016 global rise of nationalist populism to the 2020 Great COVID Lockdown to the 2022 Russian invasion of Ukraine and supposed assault on the U.S.-led political economic empire or world order, the current phase of humanity's ideological evolution suggests the defining and unifying crisis for humanity is no longer food shortages (like in the population phase) or inefficiencies (like in the productivity phase). It is now an existential question that asks what kind of globalized world we want to have (and more fundamentally, if there are any unifying beliefs that can even bind us together anymore as a world to reach that vision). Without a common destination and road to it, it is unclear how any social unit can remain together for long (whether a nation or healthcare system).

The current phase of humanity's ideological evolution to its current crisis of purpose played out in the '21st century War of Ideologies' in which the capitalist liberal democratic model of political economics (championed by the United States) "won" against not only the WWII fascism of Hitler's Nazi Germany and Mussolini's Italy, but also the Cold War communism of the Soviet Union (Kurth, 1999; Monlezun, 2022). The competing political economic models argued for (and in some respects radically) different accounts of human purpose according to dueling definitions of human nature, community, desires, needs, and goods (including questioning if such goods or good exist). To keep our focus on the key aspects of political economics relevant to AIenabled healthcare systems, we will focus on the high yield points (which does not do justice to the rich diversity of the world's peoples, but this focus is required for the sake of space). In premodern times, peoples from Christian Europe to the Muslim Middle East to Buddhist, Confucian, and Hindu China and India largely shared core beliefs, ones that could be articulated in terms of Aristotelian metaphysics and natural law ethics. Peoples held common metaphysical or religious beliefs about the nonhuman or divine origin of the universe and people by God or a supreme being, which then informed their beliefs about human nature and community which thus informed their political and economic arrangement of their social units ordered toward the good proportional or proper to their nature. These units better approached happiness, justice, and peace by living in accordance with naturally knowable objective truths such as to do good and avoid evil, which thus helped bring about the conceptual development of the individual and nation (or social unit) as a more complete or "perfect" version proper to the human individual and community. Modern political economics in Europe emerged progressively in the 17th century building from the Protestant Reformation and then philosophical Enlightenment onwards (capitalizing on the Scientific Revolution and ensuing Industrial Revolution) as a break from (or revision of) the premodern or classical tradition principally and historically embodied by the Catholic Church (via Thomistic-Aristotelianism that sought to synthesize the world's philosophies and religions).

Rejecting the classical metaphysical foundation of societies or social units (asserting a foundational reality of objective truths individually knowable and subjectively experienced), this newer modern tradition began articulating belief systems more as ideologies as a collection of constructed ideas increasingly emphasizing the material, imminent, scientific, and political economic dimensions of human experience (while de-emphasizing the immaterial, metaphysical, philosophical, and religious dimensions) (Kurth, 1999; Monlezun, 2022). The classical, unifying, and integral vision of the human person as a member of the human family (philosophically, scientifically, politically, and economically) diversified by various human social units was supplanted by the modern narrower vision (mostly or exclusively scientific, political, and economic) of diverse accounts of humanity dividing diverse social units. Liberalism was the major left-wing political economic system or ideology which was articulated philosophically as the individual being a rational autonomous agent, politically as liberal democracy, economically as capitalism, and historically as the United States and Britain along with France. Liberalism contrasted with the right-wing ideology of conservatism (and its more extreme formulation of fascism) which was articulated philosophically similarly to liberalism (largely with the individual without a higher transcendent good defined and generated by divine origin and authority), politically and economically as increasingly state-led limitations on societies to protect "traditional" constructed values and identities, and historically as Hitler's Germany, Hirohito's Japan, and Mussolini's Italy. Finally, socialism (with its more extreme formulation of communism) was the minor left-wing alternative to liberalism which was articulated philosophically similar to the above ideologies, politically as social democracy, economically as post-Marxist socialized capitalism, and historically as the Soviet Union and contemporary communist China and North Korea.

This brings us to our current political economic challenges dividing and driving much of today's societies and their embedded healthcare systems. Timothy Snyder, The Richard C. Levin Professor of History at Yale University, proposes that the emblematic politician economic cumulation of this transition point in humanity's ideological evolution is the 2022 Russian war on Ukraine, which ultimately "is about establishing principles for the 21st century" (Snyder, 2022). Those manifested by Ukraine as "the principle of self-rule" in a "democratic future" in which the "principle of sovereignty" means respecting peoples' right not only of "choosing one's own rulers but also respecting the equality of states." As of the writing of this book, such a belief system is facing off against what Snyder terms the "aging tyranny" of Russia and its premodern imperial "genocidal policies" in which there are no objective truths or common (metaphysical and) moral systems uniting a people or societal unit. There are only common beliefs (or rather convictions) in the structures of power enabling the stronger to dominate the weaker through force. Synder invokes such democratic principles in modern Ukraine as those

expressed from Ancient Greece (and more recently in the 18th century founding of the United States) upon common "self-evident truths" (i.e., metaphysical principles naturally knowable by reason about the equality of all people and their "unalienable rights" "endowed by their [common] Creator" and protected by governments with their "just power [derived] from the consent of the governed") (National Archives, 2022). In line with this ideological conception, the International Court of Justice of the UN, spanning the 195 nations of the world, ordered Russia in March of 2022 to halt its invasion of Ukraine not just for its widespread brutality against civilians but also for what the ICC described as baseless Russian allegations of Ukrainian genocide against native Russians in Ukraine (UN, 2022a). The International Criminal Court (ICC), spanning 123 signatory nations, confirmed the month prior it had sufficient "reasonable basis" that both "war crimes and crimes against humanity" which includes genocide was committed rather by the Russian state against the Ukrainian people to thus allow the ICC to proceed with an investigation (ICC, 2022).

The 21st century thus far appears to be reframing the ideological wars of the 20th in which the absence of a unifying moral system, language, and identity among the world's human social units is replaced by divisive violence in which power supplants truth, attacking not only people but also even words and ideas (i.e., up to not only attempting genocide against a people but against attacking even the reality of genocide or reality itself as simply weaponizable words and ideas). As the above evolutionary biology section introduced, political economics is the supra-(societal) structure that manifests, institutionalizes, and unites the foundational sub-(metaphysical) structure of the common beliefs of a people, holding them together on a shared existential road and destination (while detailing the cooperative terms internal to a social unit and how it externally competes with other social units, particularly those with greater differences in their underlying belief system). What is particularly defining about this latest phase of humanity's ideological evolution is that potentially for the first time in history, a growing majority of the world's nations explicitly assert a unity of purpose and identity, an international social unit of a "common humanity" to address shared challenges, including those urgent and existential crises ranging from extreme poverty and health inequalities (as noted by the UN above) to rogue AI, nuclear warfare, climate change, and pandemics (Monlezun, 2022). Such competing political economic systems globally thus shape healthcare systems at the national and local levels given the lack of international ideological interoperability, undermining the value supply chains, biotechnology, biomedical research, financing, and PubHealth critical for healthcare systems' operations (and particularly in their AI-transformation). Such systems need a minimum degree of ideological interoperability for its macropolitical economics, similar to how basic data interoperability is practically necessary for AI-enabled Big Data linking the global digital healthcare ecosystem (which we will explore possible solutions

7.2.2 Micropolitical economic forces pressuring healthcare system redesign

purpose, and thus rules and steps to get to this shared destination.

These macropolitical economic ideological forces contextualize and frame the micropolitical economic (financing) forces that further intensify the need to revisit the design for the optimal future model for healthcare systems. The local political economic factors within healthcare systems inform the ultimate desired ends and values (and thus the instrumental strategy, operations, governance, and financing at the organizational and direct patient care levels). We will shortly analyze AI ROI in healthcare system financing as a means to improve the effectiveness and efficiency of system operational achievement of strategic aims. But first let us consider the big picture in which i.e., System A deliberately prioritizes higher income and better-insured patients with less healthcare needs. They can finance more expensive diagnostics, technologies, facilities, and specialty services—but at the societal cost of increasing healthcare disparities by shunting resources away from lower income, worse insured, and sicker patient populations (and shunting such patients to System B). Like physicians must triage patients and patients' needs in order of most clinically urgent, systems triage political economic values and thus how to finance their daily operations as the means to their overarching strategic approach to their ultimate desired ends (i.e., vision of health and to whom they owe what kind of healthcare). Such finance pressures are notably embodied within the concept of UHC or the equitable access of a population to timely essential healthcare. The UN, created and dominated ideologically since by the liberal capitalist democracies of the United States and its WWII allies, asserted UHC in 2019 as not only a human right but also a societal requirement for political stability and economic prosperity, to the point that the UN set achieving by 2023 global UHC as an SDG (UN, 2019).

It is a widely shared feature of nations the world over to provide some degree of universal public education given the empirical evidence and ethical belief that it is a necessary societal good, as it is due to a states' peoples and it generally delivers significantly greater collective ROI (i.e., greater economic productivity, political stability, decreased crime, etc.) than its minimal marginal costs (i.e., taxes) (McClure et al., 2017). Similarly, UHC is framed by its proponents as a necessary societal good including for its political economic advantages (not only at a macro scale for societies, but also at a microscale for systems). It is cheaper and easier to finance healthcare systems when they have healthier populations to care for as resources can be focused on more

affordable and effective preventive rather than acute care measures generating larger societal dividends. More consistent, longitudinal, and equitable access to healthcare can better preserve a higher baseline health for populations who thus can be a more peaceful and productive workforce lifting a nation's GDP and its related ability to finance systems (in addition to the welfare of the young, sick, disabled, and elderly). Healthcare financing is political for it requires the collective will of a critical mass of a population (encompassing diverse institutions and stakeholders) to allocate resources (and their related responsibilities and benefits). But it is also concurrently economic for the content of that distribution relates to resources that are valuable goods and services which are generated and traded in the larger economy. Further, politically unfavorable or economically underperforming approaches to financing can hold healthcare systems back from performing at their optimal level delivering the sufficient value expected by their patient populations.

Explicit political economic analyses thus are increasingly recommended as a critical component of healthcare financing reform enabling healthcare system transformation (Sparkes et al., 2019). It allows a practical understanding of the relative power, position, and priorities within a society or healthcare system's political economic structure (spanning external, beneficiary, bureaucratic, budget, and leadership actors). Effectively managing the political economic competitive tensions and collaborative opportunities can empower the needed improvements in the interdependent effective technical process of that transformation. As the U.S. healthcare system (as a national decentralized network of local systems) continues to rank at the bottom of high-income nations, it continues facing political economic pressures to shed its not so illustrious distinction as the only developed nation without UHC amid its ideological radical individualism (Schneider et al., 2021). Failure to address macro- and microlevel political economic challenges and opportunities appears to thus undermine not only healthy functioning of healthcare systems now but also their capacity to undergo the AI-enabled transition into the healthcare systems of the future.

7.3 Sustainable political economic design of Al-enabled healthcare

Now that we have considered the historic and technical evolution of the political economics relevant to healthcare systems, we will focus on the (a) strategic, (b) structural, and (c) adaptive features of the emerging model for sustainable AI-enabled system design. We will then be able to move on to the specific political economic solutions attempting to successfully deploy and improve iteratively on that design.

7.3.1 Strategic features: inclusive globalism

Strategically, inclusive globalism rather than narrow nationalism appears to be a central necessity of sustainable political economic design of AI-enabled healthcare systems. The UN Secretary-General António Guterres' 2021 address to the WHO-joint sponsored World Health Summit articulated this in the context of the COVID-19 pandemic demonstrating the scientific and ethical need for a "One Health" approach to system redesign (Guterres, 2021). He argued that the pandemic revealed how healthcare systems "fail[ed]" and thus must focus on "strengthening primary health systems at the local level and achieving UHC" so they can focus on successfully responding to current population needs and "preventing future health emergencies" (including future pandemics). Central to such enhanced system design is a globalized approach linking systems' local and international dimensions and efforts to resist narrow nationalism political economic forces, as in the case of "vaccine nationalism and hoarding [which] are putting us all at risk" according to the Secretary-General. Aside from the ethical failure violating what "every person deserves," the scientific and empirical research demonstrates that such nationalism increases preventable deaths, "shattered health systems," economic collapse, and environmental pressures generating more communicable and lethal pandemic viral variants.

Narrow nationalism means prioritizing a nation's people at the expense of other nations but in a way that ultimately undermines all nations including ones own (as the world's peoples are deeply interconnected and interdependent politically, economically, and culturally). Inclusive globalism means prioritizing a nation's people while protecting the minimum mutual benefit shared with other nations. Kenyans, Americans, Chinese, and Ukrainians are not just Kenyans, Americans, Chinese, and Ukrainians—they are also global residents of a common planetary home, vulnerable to AI-accelerated disruptive technologies, pandemics, nuclear wars, and climate change. The Israeli historian, Yuval Noah Harari, observes that a modern global identity is increasingly evolving to face such "global existential threats" individual nations cannot, similar to how premodern "national identities" developed as individuals had to unite to solve problems local tribes alone could not (Harari, 2018). In the 21st century, we cannot practically deglobalize our already global ecology, global economy, and global science. But we can globalize our "national politics" without sacrificing patriotism according to Harari, for "patriotism is about taking care of your compatriots." But in our current globalized world, the only way to "take good care of your compatriots" is to "cooperate with foreigners," so Harari argues "good nationalists should now be globalists."

The 2020 Deloitte political economic report on AI in European healthcare systems accordingly projects that systems' cooperative adaptation of AI can annually save 403,000 lives, \$212.47 billion, and 1.94 million provider hours in Europe alone through such AI applications as robotics, wearable remote monitors, and telehealth-based virtual health assistance (Biundo and Strübin,

2020). Technical barriers are not the primary problems to realizing such system solutions and related societal benefits, but rather achieving a globalized political economics to deploy and scale those solutions. Deloitte highlighted that "unbiased, robust, and safe AI" requires international cooperation sharing a fair, effective, and efficient interoperable data architecture, legal and regulatory framework, health education (empowering justified public trust), and financing mechanisms. Building on the reality of the current AI arms race introduced in the AI healthcare chapter, global cooperation is required to balance the need for intellectual property protection for AI producers with the need for AI-enabled healthcare by systems (who cannot achieve economies of scale in AI-enabled healthcare delivery without coordinating technical resources). Demographic implosion in the Global North (the primary AI producers internationally) as introduced in the PubHealth chapter only further underscores the importance of globalized political economics in sustainable AI-enabled healthcare system design. The primary driver of political economics (namely, the population) is faltering in the very regions where the technology is being developed at least for the foreseeable future (enhancing the need for improved system efficiencies to replace to some extent the declining provider workforce for systems and nations' workforces who pay for them).

Despite the decades-long bipartisan nationalist foreign policy of the United States, it is still taking such progressive steps toward a globalism approach to political economics (including for healthcare systems) as promoting "friend-shoring," paired with "sustainable domestic production" as part of "supply chain resilience" for key industries, particularly pharmaceuticals for healthcare systems (Sullivan and Deese, 2021, p. 8). In contrast to offshoring (outsourcing parts of the supply chain to cheaper foreign markets based on typically who is cheapest), this friend-shoring refers to a globalized approach to building on the interdependent relationships of compatible or common political economic systems (including national security as the net sum of political stability and economic prosperity) and cultural values (united in a common foundational ideology). This approach produces goods and services collaboratively in the international supply chain network (of likeminded partners) that cannot as feasibly be done onshore or domestically alone. This pragmatic approach seeks to preserve globalization benefits in the face of perceived prohibitive costs from rising ideological divides (such as the liberal democratic capitalist nations in the West [i.e., the United States, Canada, Europe, Japan, South Korea, and Australia] vs. the more centralized or autocratic run capitalist nations in the East [i.e., China, Russia, and Iran]).

7.3.2 Structural features: democratic welfare model and disparities

Structurally, there are emerging key practical traits within a globalist strategic framework to effectively address the above disparity and demographic challenges, while preserving systems' existential need for self-determination (to

respond to the health needs, cultural values, and political economic reality of their populations and constitutive providers and partners). A 2019 systematic review of 4912 review citations demonstrated that PopHealth (including mortality, morbidity, and self-rated health) is optimized by the world's top performing nations' healthcare systems that are embedded in the political economic structure of social democratic welfare states (with increased public spending [prioritizing preventive, maternal, child, and worker health] and related decreased health disparities) (McCartney et al., 2019). In contrast to a social democratic welfare model like in Europe, worse PopHealth appears to occur with a "neoliberal" structure like in the United States in which the common good (of a people with pluralistic moral systems and varying conceptions of the objective good nonetheless are shared duties to the community) is subordinated to individual freedom (in the form of license unrestrained by external restraint) and related noninterference (for individuals and organizations 'free' from cultural, economic, and political constraint) (Carugati and Levi, 2021). The democratic welfare model in contrast additionally prioritizes a balance of medical care (including enhanced access) and PubHealth (including system operations being complemented by mandatory public education, affordable quality housing, safety policies, fair trade, and microfinance programs particularly in low-income nations) (McCartney et al., 2019). Such structural design features attempt to coordinate and streamline otherwise disparate strategic ends of various sectors and stakeholders in a nation's political economic structure (including PopHealth, PubHealth, public, macroeconomic, and governance policies).

Particular moral and pragmatic parameters appear to bound this political economic structure overarching healthcare systems. There is a growing international push for a "moral political economy" design for states (and thus for healthcare systems) (Carugati and Levi, 2021). This term concept describes how individuals and populations should act by recovering a classical and early modern "comprehensive understanding of economies, governments, societies, and their moral foundations" rather than the current late modern framework "dominated" by "economics alone." Carugati from King's College London and Levi from Stanford University articulate this movement by noting that modern politics economics emerged from Smith onward as a way to understand the "frameworks that have always organized human societies" in the form of "rules and institutions that govern and guide" individual and collective "choices and actions." Though "politics" (referring to the overarching social hierarchy of power ordering relationships among individuals and populations through policies and laws) largely have been highlighted in contemporary debates driven primarily by economics (using politics as its extension), it is the "moral" foundation of such frameworks that articulate and defend the "norms, values, and goals" (about reciprocal rights and duties related to a more fundamental metaphysical conception of the person and community united by the common good) generating, sustaining, and modifying those frameworks,

which have largely neglected to the detriment of significant improvement on pressing societal challenges as noted above. Such proponents of recovering a comprehensive "moral political economy" seek to support such a position by pointing to modern evolutionary biology, history, anthropology, classical moral philosophy, and empirical evidence about the increasing political instability, economic decline, and societal divisions in the modern international political economic structure dominated by U.S.-led neoliberalism as noted above. Recovering the long-running and global common moral sense of the human individual as a person (a social interdependent embodied animal with duties to the community and common good, rather than simply an autonomous disembodied decision-maker with rights to self-defined individual goods) is thus key to creating a more sustainable political economic structure.

Yet this moral recovery must operate in tandem with the concurrent trend in modern political economics to understand pragmatically not just what people should do but what they actually do. Such political economic research particularly in "public choice theory" within healthcare systems highlights how patients as citizens act collectively through economic and political demands in a way that shapes the design, strategies, operations, and reform of healthcare systems (Costa-Font et al., 2020). This public choice draws on game theory and the mathematical work from the Nobel Prize-winning American economist, James Buchanan, by empirically observing how politicians in a self-interested manner create, modify, and act according to constitutional (i.e., rules of the "game" that is politics) and policy measures (i.e., ways to play the game) to sustain and enhance their power, even to the detriment of the common good or net societal benefit (Buchanan and Tullock, 1962). Even through deficit spending (spending more on societal projects than what taxes collect), politicians are incentivized according to this theory to manipulate public choice to increase their votes for the perceived value of such societal benefits including welfare and local projects to more efficiently allocate societal resources (even if they do not provide greater actual societal net benefit). Accordingly, Costa-Font et al. demonstrate that such a political economics theory helps explain how healthcare spending is becoming one of the most rapid sectors of public spending globally (even when increased spending occurs without proportionally improved outcomes, let alone ones that are affordable). A "moral political economics" informed public choice approach to healthcare system design therefore in a social democratic welfare state structure may thus help orientate public support for higher net benefit system performance by constraining political and economic actions for not just individual but also the common good (translating practically into improved healthcare effectiveness, efficiency, and equity by incentivizing public choice for actual value and thus for politicians to deliver it).

7.3.3 Adaptive features: affordable AI ROI

Adaptively, sustainable political economic design of AI-enabled healthcare requires effective analytics to drive iterative and adaptive financial decisionmaking. We have already considered strategic and structural considerations about the overarching political economic dimension of healthcare systems. But to advance toward greater societal benefit (individually and collectively), improved utilization of such political economic metrics as ROI and qualityadjusted live years (QALY) may be required to accelerate that progress by real-time assessment of the rate and direction of progress (or lack thereof). To marshal the political support and economic resources required for AI-enabled healthcare systems, AI must first be shown to have net benefit (and preferably a greater net benefit compared to alternative solutions in the form of greater benefit at lower affordable cost). ROI is a popular and prevalent tool to determine such decisions in multiple economic sectors. Yet there are no published, peer-reviewed, complete cost impact analyses on AI adoption thus far in healthcare (as of a 2020 systematic review whose conclusions have thus far not been contradicted as of the publishing of this book) (Wolff et al., 2020). This review demonstrated that the few studies which attempted such cost analyses failed to sufficiently calculate the operational costs and initial investment for AI services and infrastructure, in addition to the costs for comparable alternatives to determine the most efficient option. Without such ROI considerations, systems can be shooting in the dark with a lack of coherent approach to systematic AI introduction and scale-up within healthcare systems. Simply throwing money at a problem is not a solution, especially when the possible solution is something as potentially complex and costly as AI-enabled healthcare.

Subsequent work has sought to improve such an ROI approach to improving the adaptive design of AI healthcare to make progressively smarter decisions (Rao, 2021). In general, ROI is a core economic principle guiding political calculations: understanding what you get for what you pay (and ensuring it has more net benefit than alternatives). AI ROI in particular can be calculated as the following:

 $Return \ (Model \ benefits \ [number \ of \ predictions \times value \ per \ prediction] - Benefit \ uncertainty \ [Error \ cost \times impact])$ Investment (Required resources × cost per resource)

Quantifying returns and investments requires conceptualizing their hard and soft dimensions including. Hard returns are decreased time and cost with increased productivity and revenue. Soft returns are improved product, service agility, skills retention, and experience. Hard investments are licenses and resources, while soft investments are training, experts, analytics, storage, and data acquisition. Primary challenges to implementing healthcare AI ROI include underestimating the uncertainty of benefits, narrowly defining time-specific rather than lifespan returns and investments, and treating AI projects individually rather than as synergistic components in a product portfolio adding value to the entire system.

Amid competing moral values and political economic incentives in today's pluralistic healthcare systems (which can challenge otherwise straightforward ROI calculation focused on net economic benefit), quantification of net health economic benefits may require additional methodological development such as with QALYs. This metric began as a dominant economic tool that has since become a cornerstone of healthcare decision-making by representing the mathematical product of quantity and quality of life (jointly considering interventions' morbidity and mortality impact) (Whitehead and Ali, 2010). Like in ROI analysis, QALYs can be considered as the empirical health "returns." It thus facilities comparison at the macro and microlevels of political economic discussions for healthcare systems to not only maximize the greatest population net benefit with the available finite resources, but also to adapt system designs and related strategies and operations to better respond to changing individual and population needs, values, and resources. Contemporary research has sought to further improve QALYs ability to more defensively capture equity and pluralism in the theoretical dimension (including weighting calculations by equity and representing the range of valuations of health conditions), while the practical dimension shows its prevalent and high-level utility as a decision-aid tool, evidenced by the UK's National Institute for Health and Clinical Excellence (NICE) mandating QALY's use for health technology analysis. A 2022 study further demonstrated the emerging trend of QALY utilization to facilitate political economic consensus in healthcare AI at the system level by specifically showing how AI-driven risk prediction of breast cancer followed by no breast cancer screening for low-risk women is the most cost-effective population health policy (with an incremental costeffectiveness ratio of \$23,755 per QALY gained) (Mital and Nguyen, 2022).

7.4 International political economic models of Al-enabled healthcare: nationalized, privatized, and globalized

Let us now synthesize the theoretical background thus far so we can examine international political economic models of AI-enabled healthcare and then the real-world examples within them that represent the range of projected healthcare systems for the future. We have considered how healthcare systems operate by, through, and because of their overarching political economic structures which are contextualized and animated by their underlying diverse cultures (manifesting the common underlying beliefs about the nature of humanity, the individual, and the community). Differing foundational moral beliefs and values (about what is good, healthy, and fair) informs the political determination of society's economic arrangements that prioritize limited resources to balance the biggest drivers of healthcare costs (i.e., labor costs [particularly demographic decline-related labor shortages], technology, pharmaceuticals, liability, regulation, and undermanaged PopHealth [with typically lower insured and income individuals costing systems significantly more expensive healthcare utilization and resources]). Systems thus require complex cooperative competition in the political economic dimension, encompassing regulatory and liability structures politically in addition to paying patient populations and supply chains economically (external to their systems which include biotechnology and pharmaceutical companies, supply companies [i.e., for surgical supplies, building equipment, accounting software, cleaning agents, etc.], EHR companies, and marketing and online companies). And all this sums to produce an operating margin for healthcare systems which must compete with other systems (even when nationalized) on providing better quality or cost or both in terms of composite equitable value (or at least compete on the basis of marketing-driven perception) for patients populations (as systems compete especially to attract either higher income and/or insured populations who use less healthcare, or sufficient critical mass of lower income and/or insured populations to produce economies of scale sufficiently lowering nonreimbursed or charity expenses).

We have additionally considered how modern history demonstrates the technological innovations central to Industrial Revolutions accelerated the ability of their primary state adapters to outcompete other states and so exert disproportionate influence on others at the international level. The current Fourth Industrial Revolution (centered on AI-driven cyber-physical systems shaping adaptable global value-chains) already illustrates the global race for the most rapid and efficient societal AI adoption through power players and states leveraging shared intellectual property, trade, and power (political economically, including its military and cultural dimensions) to advance their individual, competing, and cooperative interests. Demographic decline in the Global North (culturally and ideologically differentiated into the US and European and Pacific ally led West on one side, and China and Russian-led East on the other) accelerates the AI tech and arms race. This is particularly acute in healthcare systems where exploding healthcare costs, growing prevalence of older populations utilizing more healthcare, political instability from growing polarization and widening inequities, and need for maximized labor efficiency only heighten the need for AI to provide commensurate value add, while maximizing efficiency, equity, compliance, and productivity at the scale and speed demanded by the emerging stark challenges of the future (that are already here). There are three prominent state-level models of AI-enabled healthcare political economics to solving such problems: nationalized, privatized, and globalized.

7.4.1 China: centralized nationalized model

China merges Marxist-Lenin communist political centralization and capitalist economic decentralization (or "state capitalism") under the increasingly autocratic concentration of power under President Xi Jinping's Chinese Community Party (CCP), after its initial post-Mao Zedong era attempts

through Deng Xiaoping to institutionalize "authoritarian resilience" against such trends (Bardhan, 2020; Shirk, 2018; Bremmer, 2010). This unique model among other developing nations like India does endow China with notable strengths of strategic, united, decisive action such as through efficient central command (of top-down command wielding effective local economic development), career incentives driving local growth, and sustained longitudinal strategic programs (i.e., health system development, poverty reduction, societal welfare, and mass industrialization and education). Related structural weakness in this political economic model includes institutionalized corruption and static strategic vulnerability. Party loyalty including explicit longitudinal plans can undermine transparent accountability, checks on power abuses, necessary dissent and debate, sufficient performance, and ultimately societal resilience to external and internal shocks as inhibited information flows hamper effective collective adaptation to such crises. An often-cited historical example of such dynamics is the 1959-61 Great Famine which researchers within and outside China considered principally a "manmade catastrophe," humanity's largest famine, and the cause of death for 30 million mostly peasant Chinese citizens (Smil, 1999). Zedong as the founder and first president of the CCP (and the modern Chinese state under the title of the "People's Republic of China") ordered under the Great Leap Forward the mass mobilization of the nation's large populace through rapid industrialization (making farmers into steel production workers) with local CCP officials significantly overinflating local communal farming yields, resulting in mass starvation. In contrast his successor, Xiaoping, through his capitalist economic reforms opening China to the world orchestrated what the World Bank has since recognized as the most rapid sustained growth of any economy in history, lifting nearly 100 million out of poverty in just 4 decades (Vietor and Galef, 2017).

This political economic momentum frames China's nationalized and centralized healthcare system, including its translational healthcare AI from research to practice at a faster rate than the United States (which taken together, these two states account for 90% of all health AI start-ups internationally) (Olcott, 2022). Political and economic centralization facilitates health information centralization across the entire nation, in contrast to the United States where local healthcare systems have financial, regulatory, and technological disincentives for such data sharing (though there appears to be more prevalent unofficial sale of Chinese patients' health records and unreported data breaches in contrast to the traditionally more protected U.S. records and stringent regulation). Such AI-driven efficiency gains are increasingly prioritized in Jinping's power centralization reforms given the looming threat of the "middle-income trap," describing wage stagnation hindering a developing middle-income nation such as modern China from becoming a developed high-income nation. In this trap, wage increases and growth potential in an export-driven low-skill manufacturing-dependent country are exhausted before

it can transition into innovative, efficient, higher-value production that is competitive with high-income nations (Deloitte, 2017). As China overtook Japan in the 1990s as the primary Asian economy (becoming the largest global GDP driver into the 2010s), India is projected to dethrone China by the end of the 2020s as China remains on track to get older before getting rich (while India adds 115 million more and better-educated workers through the mid-21st century and China's population implodes to less than half of its current levels by 2100) (Vollset et al., 2020). Such demographic challenges supercharge political economic pressures for AI-enabled healthcare systems to make up for efficiency gains that it increasingly lacks in its shrinking workforce and funds to care for a growing aging population with greater healthcare needs.

7.4.2 UK, India, the United States: democratic nationalized and privatized models

Empirically and by consensus (including a 2011 summit of representatives from 95 nations), democracies on average sustainably produce superior integral human development than autocracies (and other competing political models), as democracies typically have greater decentralization of political economic and cultural power, information flows, and accountability allowing more effective collective adaptation to complex and changing crises than when the political structure centralizes power in the hands of a few who are less accountable to the many (Acemoglu et al., 2022; IDOS, 2011; Sachs, 1999). As articulated by multiple Nobel Prize winners in positive sum game theory, such a model compared to alternatives better enhances the likelihood of individuals' needs and desires being satisfied in a win-win or positive sum societal arrangement of collective health and wealth generation (in contrast to a zero-sum game where winners are only created at the expense of losers) (Gul, 1997). Proponents of this political economic system point to how constitutional liberal democracy (with its primary economic manifestation as the related free market capitalism) has produced history's most enduring governance system by translating its vulnerabilities (attempting the difficult balance protecting individuals and minority groups with responsiveness to the majority's will) into sustainable resilience (enabling self-critique, nonviolent reform, and ultimate adaptiveness to dynamic crises and challenges) (Galston, 2020). The Harvard and Columbia economist and UN Sustainable Development Solutions Network Director, Jeffrey Sachs, noted the empirical and historical evidence for the unprecedented success and dynamism of this political economic model's capitalism (to the point that it become the primary model globally for nations by the 1990s) (Sachs, 1999, pp. 96–98). From the 1980s onward, China, Russia, India, Turkey, and states across Eastern Europe, South and Central America, and East Asia progressively moved away from postimperial socialism or state-led industrialization to free-market models (particular with its fundamental features of private ownership and marketbased transactions of an economy's core sectors, in addition to concurrency convertible and shared standards for global trade [as noted in the World Trade Organization's agreements spanning 120 member nations]).

The constitutional liberal democracy underlying contemporary global capitalism was championed by the United States in the wake of the post-WWII world as it created an international political economic structure reflecting its own. This model would be embedded and enshrined in the UN's political structure (with its moral foundation rooted in the classical Thomistic-Aristotelian virtue ethics and modern Enlightenment rationality articulating a common morality from a common humanity, including the latter's derivative individual dignity and thus rights and duties to the common good as manifested in the UN's "constitution" of the Universal Declaration of Human Rights [UDHR], which became the foundation of international rule of law) (Monlezun, 2020, 2022). This political economic model was invoked in 2022 by the majority of the world's nations through the UN as a modern prosovereignty, pro-self-determination, positive-sum globalist alternative to the premodern imperial, autocratic, zero-sum nationalist model manifested in Russia's invasion of Ukraine (even with China and India by late 2022 emphasizing their growing concern for the war) (Ignatius, 2022; Foy et al., 2022). This unified response followed the 2015 adoption by the world's nations of the 2030 Agenda for Sustainable Development as a "shared blueprint for peace and prosperity" (UN, 2022b). It consisted of 17 SDGs in which "inclusive and sustainable economic growth ... for all" recognizes explicitly that "democracy ... and the rule of law ... are essential" for global integral human development. Following the Soviet Union's collapse up to 2015, the global adoption of such political economic features of free market reform in a democratic-dominated world order from 1990 to 2015 witnessed a 26% surge in the world's population or 1.1 billion rising from poverty as the modern postimperial world industrialized, digitalized, and globalized (UN, 2022c).

These structural and historical trends are embodied in healthcare systems in democratic political economic structures diffusing power through a more decentralized network of stakeholders, while retaining a degree of a hierarchical network for command and control of resources and adherence to a unifying system of strategies, laws, regulations, standards, and norms (generated from and sustained by underlying common beliefs and values). The U.S. Operation Warp Speed (OWS) is highlighted as an example of this model's comparative strengths. This 2020-21 public-private partnership under President Trump produced, tested, approved, and distributed on scale two commercial vaccines in just 8 months (with historic speed, effectiveness, and safety) in what the New England Journal of Medicine described as "miraculous" (Shulkin, 2021). OWS united healthcare systems, universities, pharmaceutical companies, government agencies, and the military to translate collaborative cooperative competition into its RAPID operational framework: Results orientation, Agile development, public-private partnerships, Interest

alignment, and Diversification. OWS pitted eight companies against each other to deliver the best vaccines while harnessing innovation, distributing responsibilities, processing in parallel (including vaccine design, testing, and production in parallel rather than sequentially), and leveraging individual and collective conviction of united purpose (likened to when President Kennedy, who launched Project Apollo, stopped during a NASA tour to speak with a janitor mopping the floor, asking him what he did—"I'm helping put a man on the moon!"). The weakness of this model can be seen in the radical individualism and political polarization of the pandemic particularly prevalent in the United States, its vaccine nationalism noted above, and the struggle of the model's leadership structure to unify competing groups differentiated by significantly different degrees of power (as seen notably in the January 6th Attack on the Capital when over 2000 Trump supporters stormed the capital to stop his Vice President Mike Pence from certifying the electoral college votes that would ultimately confirm Trump's defeat to President-elect Joe Biden, though model proponents point to this stress test as evidence of its resiliency to survive even that crisis) (DOJ, 2022). Backed by the 2022 UN Secretary-General, the US political scientist, Ian Bremmer, has articulated this general historical trend of adaptive resiliency with the political economic "J-Curve," in which political stability (y-axis) initially and temporarily decreases as states move toward greater societal openness (x-axis), before steadily increasing past the inflexion point (as more closed and autocratic leaders lose control as states supposedly "modernize," open, and democratize), while the entire curve can shift up with stronger economic performance (Bremmer, 2006, 2022). Within this political economic model of capitalist democracies, there is a range of healthcare systems from the nationalized to the privatized ends of the spectrum for healthcare delivery and financing.

The WHO Director-General in 2022 asserted that COVID-19 is a "health crisis ... [that] requires a whole-of-government [WoG] and whole-of-society response [WoS]" (Ortenzi et al., 2022). This inclusive or moral or local globalism approach emphasizes the decentralized and interdependent aspects of the above overarching political-economic model requiring multi-sectoral collaborative competitive competition, as the same approach underlying the SDGs, seeking to constrain an otherwise laissez-faire capitalism within a moral framework of individual liberty safeguarding communal equality by orientating it to the common good, and operationalizing it in a public—private partnership run on individual agency as seen with OWS. Thus, healthcare systems like their overarching societies are structurally incentivized in this model to maximize not simply profit at all costs, but efficient and equitable societal benefit without sacrificing the individual. Yet like the historic tension between equality and liberty, the democratic model features a spectrum of how to optimally balance patient and population needs. For instance, though the privatized U.S. healthcare system is a world leader in biotechnology innovation and effective acute medical care (whose proponents argue ultimately

benefit the world and poor through eventual diffusion i.e., COVID-19 vaccines), it has among the worst affordability, access, efficiency, and equity at a population level among high-income nations—despite spending the most to get the worst outcomes (Schneider et al., 2021). There is additional concern about worsening quality and cost following Obamacare's attempted healthcare reform which inadvertently intensified regional monopolization and bipartisan attacks (with reduced competition and thus quality and affordability), though the U.S. system proponents argue its multipayer public-private mixed market has achieved nearly universal coverage, comparable to Switzerland or Germany, while still demonstrating notable areas in which sustainable and successful structural fixes can still occur (i.e., through capitated risk-adjusted and managed care funding mechanisms for the private-public mix of providers) (Kacik, 2017; Miller and Moffit, 2020). The model is proven and promising, not fatally flawed so the argument goes. The persistent challenge in this privatized model has been aligning a critical mass of stakeholders (payors, providers, patients, government, academics, and corporations) to shared strategic goals allowing efficient and equitable unifying operational frameworks for care delivery standards, funding mechanisms, and regulations.

The UK on the nationalized end of that political economic spectrum emphasizes a more consistent WoG and WoS approach through its NHS which consistently ranks among the best-performing systems, especially in affordability, access, efficiency, equity, and safety by the UK funding and providing "free" (at the point of use) healthcare directly to its population as UHC through general taxation (Schneider et al., 2021). As the PrMed chapter discussed, the UK concurrently leverages the private sector's innovation i.e., through its Lifebit's partnership with the National Institute for Health and Care Research and the University of Cambridge in their CYNAPSE clinic-genomic cloud-computation platform to supplement its system-wide services (while avoiding the high cost of having to build out those capacities internally). UK's moral political economic model is unsurprisingly echoed in the current structures of its former colonies, the United States above and India below. In the world's largest democracy, India's Prime Minster, Narendra Modi, launched Ayushman Bharat ("Modicare") in 2018 as India's NHS, representing one of the largest publicly funded insurers by targeting 500 million belowpoverty-line individuals to improve health equity and population productivity (Nirula, 2019). Modicare explicitly attempts to address the UN SDG (particularly improved health and inequalities) through UHC, comprehensive primary care, transparent system competition by value, efficient and fair taxation and financing, and enhanced affordable access to essential drugs, diagnostics, and acute care for poor families.

7.4.3 Friend-shoring of international healthcare systems: globalized model of value blocks

This chapter considered thus far brings us to the point of summarizing key trends driving the political economic structures which frame modern healthcare systems (that are globalizing as AI accelerates their interconnected digitalization). The post-WWII world became healthier and richer as it became more democratized, capitalized, industrialized, digitalized, and globalized through increasingly dense and interconnected ideological, cultural, political, and economic networks linking individuals, communities, and nations to historic levels. Yet the 2010s witnessed rising geopolitical tensions between competing versions of capitalism (including the more decentralized democratic version of the US and the more centralized autocratic version of China) accelerated by the post-2008 Great Recession, 2010s initial Chinese-global decoupling, post-2016 US-China trade war, 2020 COVID-19 pandemic, and 2022 Russian invasion of Ukraine (and energy war with their American and European allies in addition to a food war with the Global South) (Botros, 2022; Black and Morrison, 2021; Rojas et al., 2022). The spillover cost effect of the latest example is over \$2.8 trillion in global economic damage according to the OECD (disproportionately born by the Global South, that is more vulnerable to food, energy, and demand shortages, in addition to Europe attempting to wean itself off Russian energy dependence). Additionally, as China's growth slows, population shrinks, and relationships further sour with local and former international partners, it is increasingly decoupling from the world (especially with the U.S.-led West and its allies including Europe, Japan, India, South Korea, and Australia) to prioritize their domestic market reliance and competition globally. Concurrently the West and its allies increasingly are responding with reshoring and friendshoring (transitioning to local globalism in which nations with more compatible ideologies and political economic models (particularly capitalist democracies) seek to enhance their shared and sustainable security, stability, resilience, and prosperity through more localized value-supply chains producing and trading critical goods and services.

As China decouples and the West friend shores, both blocks compete for influence on the Global South who are seeking to avoid being collateral damage to the perceived geopolitical clash between the West and East. Such global value blocks seek to optimize energy independence, short and redundant (including diversified) supply chains, and aggression deterrence by denial as prerequisites for stable domestic operations. This is particularly emphasized for healthcare systems following COVID-19 emergency as a pandemic, as systems care for the populations that sustain the overarching culturally embedded political economic structures of their nations. Biotechnological, aging and shrinking populations, and health cost explosions internationally have increasingly driven healthcare systems (like their overarching societies) to accelerate AI-driven digitalization of their systems to improve efficiency and equity to keep pace with such historic geopolitical shocks and demographic trends by complementing their comparative advantages and mitigatable weaknesses. As China seeks greater self-reliance and self-focus, the West that has significant AI healthcare IP and related institutions is nonetheless increasingly reliant on its southeast Asia and Global South partners (as

immigrants, consumers, and producers) for what overlapping moral systems articulate with the anthropological observation that "children are the most indispensable resource of the future," the most critical renewable energy and creative solution to modern crises, as there is no SDG for a humanity that has no children to continue it (Lubov, 2022; UN, 2022b). The OWS as noted earlier can be understood therefore as an early nation-wide WoS solution (increasingly exported through the network of U.S.-allied nations) responding to a global challenge (successfully in the near term for their populations), but one that has not yet translated into successful inclusive globalism sufficiently bridging the ideologically divided value-blocks (and thus that already demonstrated intermediate-term negative outcomes such as selection of variants affecting those initial states and widespread economic downturns and multiple regional political conflicts and riots). As the AI healthcare technologies and institutions noted above are increasingly bridging value blocks, there is durable optimism that there will be increasing pragmatic political economic pressure for healthcare systems to globalize in needed collaborative competition with each other and their related stakeholders (even when their overarching states fail to do so).

7.5 Local political economic models of Al-enabled healthcare: $Big\ Tech + Big\ Insurance = Big\ Medicine$?

Within the state-level political economics framing healthcare systems, there are influential local political economic trends shaping the relationship of Big Tech, Big Insurance, and their influence on the emergence of Big Medicine.

7.5.1 Big Tech digitalizing health care: "digital colonization" and "open healthcare" as horizontal-vertical integration

Big Tech, or the "Tech Giants," conventionally refer to the four largest IT companies in the US (including Amazon, Apple, Alphabet [Google], and Microsoft dominating their economic sectors, as each individually exceeds \$1 trillion market capitalization as they collectively wield unprecedented political economic and societal influence globally) (Ozalp et al., 2022; Evans and Herrera, 2022; Winkler, 2021). They have accelerated their attempted disruption and (for some proponent's eventual) domination of the healthcare sector since the COVID-19 pandemic. The \$3.6 trillion spent annually in the U.S. healthcare system alone coupled with its global inefficiency makes it a prime target for Big Tech with their immense AI-driven efficient adaptative digital domination of their sectors. Yet there were few if any sustained and substantive success stories of disruptive innovation in health care until the pandemic catalyzed an international demand for more effective, efficient, and integrated PubHealth and government responses to this health crisis through local healthcare systems. As PubHealth interventions faltered, governments

lowered regulation, and healthcare systems opened more to digital services, Big Tech moved in to fill the gap.

- (a) After acquiring an online pharmacy in 2019, Amazon in 2022 purchased the U.S. primary care clinic network, One Medical, allowing Amazon to sell direct clinical services to employers through 180 clinics in 24 states, expanding on its 2019 Amazon Care (telehealth service) and its 2017 acquisition of Whole Foods Market (spanning 500 grocery stores across North America and the UK.
- (b) Apple's CEO, Tim Cook, in 2019 declared Apple's greatest contribution to humanity will be in health, yet its initiatives have largely stalled first in its primary care clinics and then its digital health app (HealthHabit), leaving its most recent efforts up to 2022 focused on the Apple Watch as remote cardiovascular monitoring to complement traditional non-Apple healthcare delivery.
- (c) Alphabet (the parent company of Google) wants to "weave health into everything we do" according to its Chief Health Officer in 2021, particularly in its strategic focus on its cloud, search functions, and data analytics (clarifying the social determinants of health driving the majority of health outcomes) (Doniger, 2021). Its related operations therefore prioritize partnerships (including with Mayo Clinic, HCA, and Ascension contracting with the above digital services) and acquisitions (including FitBit's remote health monitors).

According to Oxford, Big Tech (and smaller companies following their lead) generally have followed a similar four step game plan for entering healthcare systems (with projected disruption at least and eventual domination at most) (Ozalp et al., 2022). They begin by providing data architecture including cloud storage and computing to systems, especially primary care providers focused on preventive care. They build on those ecosystem relationships to obtain indirect access to patients' clinical and/or financial data. They then apply their analytics to the data to generate reportedly superior insights to improve clinical and cost outcomes. And finally, they attempt to translate these insights into their own superior digital products and services to optimize existing healthcare delivery mechanisms. This process of "digital colonization" helps tech companies avoid the less profitable dimensions of healthcare systems (i.e., actual healthcare delivery) and related complex regulations, while enhancing their profits (by selling the final products and services in addition to the contracting their cloud and analytic services). Providers and payors may "own" patients, but this political economic model for Big Tech would allow them to "own" their data (becoming so embedded, ubiquitous, and "critical" that regulating or competing with them becomes not only increasingly politically fraught but economically impractical). Digital colonization economically thus functions as an efficient process of vertical integration (as the business side of Big Tech expands through partnerships and

acquisitions of other businesses operating after or before them in the supply chain [i.e., translating biotechnology, pharmaceuticals, and data into healthcare delivery into healthcare outcomes]) and horizontal integration (partnering or acquiring a similar business in the same stage of the supply chain in the same industry). Politically, this process assists Big Tech to develop public trust and acceptance of their push into health care as enablers of existing healthcare delivery (which they can then leverage into greater regulatory, government, and payor support or at least acceptance of their role not simply as an adjunct but even a necessary component of the digital healthcare ecosystem).

Similar to the UK's "Open Banking" reforms (accelerating efficient and innovative value-add to customers through third-party access to financial data through APIs), there appears to be a growing acceptance (and reliance) on nations for versions of "Open Healthcare" globally due to political and economic pressure post-COVID-19's emergence for more effective and affordable healthcare which Big Tech may be able to deliver (Ozalp et al., 2022). But there remain substantive questions about this "democratization" of health care (through Big Tech's digital health services complementing healthcare systems in the global digital health ecosystem) in a way that preserves justified patient and societal trust in such AI-enabled healthcare systems (acceptably balancing the potentially competing aims of protecting consumer privacy, keeping digital markets competitive, and delivering high-value healthcare equitably). This democratization thus depends on the political economic structures of nations to determine their collective vision for ultimately balancing healthcare value creation (seeking to ultimately optimize value-add to patient populations efficiently and equitably, which systems typically prioritize) and value capture (seeking to ultimately prioritize profit optimization, which Big Tech typically prioritizes, even if it requires avoiding certain value creation activities).

7.5.2 Big Insurance: buying all of healthcare

On the other side of this tech-enabled healthcare delivery, there is Big Insurance on the financing side of it. Most of the world's nations have some degree of UHC, with many countries' healthcare systems operating through or alongside nationalized state-backed health insurance and/or provision structures (with UHC in contrast officially absent in the United States [the only developed nation without such as already noted] and nearly a dozen developing nations [including China, Syria, Yemen, Afghanistan, Pakistan, Nigeria, Egypt, Iran, and South Africa]) (Shvili, 2020; Wagstaff and Neelsen, 2020). These national payors provide UHC in its two key dimensions of service coverage (affordable access to basic or essential healthcare services) and financial protection (avoiding undue financial hardship with such access). A 2020 World Bank global analysis of both dimensions (measured in a single UHC index score) indicated that as GDP per capita increases, UHC scores generally increase (mostly through enhanced healthcare financing through government welfare mechanisms and social health insurance). Taken together with the earlier section discussing how social democratic welfare states appear to generate the highest healthcare quality by outcomes (compared to alternative political economic structures), it appears that wealthier states become healthier through the greater collective support of state-wide funding for healthcare systems (emphasizing efficient preventive services). These states are thus big insurers.

But Big Insurance is uniquely found in the private-prioritized U.S. healthcare system (which because of the market size has an outsized influence on healthcare financing globally). Similar to how Big Tech has a vast influence on the global economy generally and the technology sector specifically, Big Insurance fills a similar role in this financing. This group encompasses the five largest U.S. private insurance companies (by annual revenue): UnitedHealthcare (\$286 billion), Anthem (\$138 billion), Centene (\$126 billion), Kaiser Permanente (\$89 billion), and Humana (\$83 billion) (Newitt, 2022). The five businesses account for nearly 50% of the health insurance sector by revenue, despite representing 0.55% of the total number of insurance companies. If Big Insurance were a nation, they would be in the top 20 richest nations on the planet, more than Saudi Arabia, Argentina, and Sweden. And as Big Tech's entry into healthcare systems has global implications, so does Big Pharmacy. As the AI overview chapter introduced, the push for vertical integration particularly for Big Pharmacy following United's Optum (leveraging their political economic position as the largest payor to become the largest provider) has triggered a gold rush in large insurance companies buying up primary care networks, hospitals, pharmacies, and other direct care stakeholders (including Humana-Kindred, Cigna-Express Scripts, and Aetna-CVS) (Jaspen, 2018). Bigger data and smarter AI accelerate more targeted and aggressive acquisitions to enhance companies' competitive advantage by exploiting political weaknesses of competitors and underexploited economic niches. Such resulting economies of scale reduce internal costs, boost profit, and bypass traditional barriers (including regulations and political resistance to "newcomers") on the way to remaking traditional healthcare systems with the emerging business model of data and political economic-driven redesigns for the healthcare systems of the futures. As the earlier section on healthcare monopolization noted, such value capture of Big Pharmacy similarly and typically does not translate into improved quality but worsened costs and inequities for patients (as these payor-provider blocks compete for higher paying and less sick patient populations).

7.5.3 Big problems in healthcare takeovers: graft (corporate) versus host (healthcare) rejection

Clinically, graft-versus-host disease is when a transplanted or donated tissue like bone marrow attacks the tissue of the patient receive it; transplant

rejection is when the receiver fights off what is transplanted. For all the advantages AI-enabled Big Tech and Big Pharmacy bring to healthcare, both types of rejection in both entities can and are occurring. Amazon can revolutionize telehealth and pharmaceutical delivery through its vast analyticdriven commercial distribution network; Apple can transform remote medical monitoring and connected apps with its Watch and Health apps; Google can translate DeepMind's best-in-class DL for translational medical research and commercialized products; Microsoft can revamp integrated medical cloud computing and health IT services (Mesko, 2022). Big Pharmacy can provide proof-of-concept and scale for healthcare systems globally for efficient and equitable public-private partnerships (when corporate innovation is paired with public funding and demand). But the challenges that continue to be headwinds slowing their entry (and preventing the entry of much of their smaller competitors) include prohibitive regulation and liability, capital competition, superficial underinvestment, and consumer-patient mismatch (Pearl, 2019; Padmanabhan, 2021). Unlike other sectors Big Tech has disrupted (from retail to entertainment to transportation, etc.), legacy or traditional competitors have greater experience in the complex healthcare environment of regulation and liability in addition to competition for providers. From the convoluted public-private U.S. healthcare system to the stringent data requirements of Europe to the shifting regulatory schemes of many emerging economies, it pays for traditional healthcare systems to have deep institutional knowledge navigating the intricate network of local, regional, national, and even international regulations and liability (this is particularly challenging for Big Tech which became big through force multiplying productivity with massive data—as healthcare data is much more stringently guarded than other data, it can quite challenging to obtain the data Big Tech needs and they are typically very reluctant to share theirs). Aside from regulations, can you sue AI? As tech companies try to break into healthcare systems, they have been thus far very hesitant to share any liability for their algorithms even if compliance is demonstrated, while governments have struggled globally to propose let alone adapt comprehensive and cohesive liability sharing between providers and the data scientists and engineering creating the AI augmenting care (as evidenced by the growing lawsuits for AIenabled surgical robots already) (Griffin, 2021). Additionally, many tech companies treat healthcare as a side hustle, leading to prolonged underinvestment in mastering the complex barriers required to enter and thrive in healthcare systems (including developing deep and productive cross-sector collaborative relationships among systems, academics, payors, and providers required to ground healthcare AI in high value-add, real-world applications). Finally, consumer demand economically is not interchangeable with patient needs clinically. Some patients may want an expensive and unwarranted MRI of the knee if they experience a mild injury playing tennis. But that does not mean it is necessarily medically required. Shifting from insatiable demand to medically indicated need can be institutionally and practically difficult especially for Big Tech given this sector-specific nuance.

7.6 "Resilient integration": comprehensive end-to-end structures

We explored in this chapter how political economic forces at the macro- and microlevel frame, influence, limit, and drive healthcare systems. Such systems require people (and thus politics), financing (and thus economics), and morality (by common beliefs about what health is and what healthcare is owed to others and oneself). We therefore attempted to understand the evolutionary biology, industrialization, digitalization, and globalization of healthcare systems as manifestations of a specific form of political economics (embedded culturally and structurally in specific places, networks, and nations) to ultimately allow us to better understand how AI is influenced and being influenced by such forces that ultimately frame the physician-patient relationship at the bedside. To optimize the efficiency and equity value-added by AI in the emerging model of the future's healthcare system, we have thus considered a "moral political economics" in which systems are embedded can be transformed into what the UN describes as "inclusive, resilient, and sustainable" (UN, 2022b). Local globalism (that prioritizes the local community, but does not pit it against the interconnected larger healthcare and human community) appears to be a promising way forward to allow systems and states to adopt the required competitive advantages of various political economic models (from centralized to nationalized to privatized to globalized) for the needs of their patient populations. (a) Cocreation and (b) resilient integration may therefore be key components of this transformation to value-based healthcare systems that fit their needed niches in their communities.

(a) Cocreation is the strategic organizational framework equivalent to the R&D design model of Trustworthy deep learning AI Co-Design introduced in the AI overview chapter. In contrast to digital colonization, cocreation is the mutually transparent, positive-sum partnership of Big Tech (and by extension Big Insurance) and healthcare systems. Both parties identify the collaborative convergence of their individual needs for strategic focus, value-creation, and financial demands in a shared framework of intellectual property management. The company can design, deploy, and optimize a personalized solution in real-time direct patient care while the healthcare system can continue its focus on value-based healthcare delivery. Both parties decide upfront which parts of the solution they "own" (including its intellectual property, larger industry impact, and responsibilities) through a cross-sector collaboration in a digital healthcare ecosystem. Cocreation pragmatically leverages the complementary needs of each party to enhance the human centered-design dimension. End-product solutions are envisioned initially as concrete answers to particular demands of patients and populations in a way that defines the desired outcome and ownership shares by each party. This

- strategic framework additionally allows concrete consideration of the macro- and micropolitical economic dimensions of the healthcare system (to tailor the AI-driven data-based solutions to patient and finance needs, according to the existing cultural and operational structure of the system).
- (b) Resilient integration" refers to the comprehensive networking of end-toend structures enabling AI to transform healthcare systems into efficient, equitable, and sustainable organizations. It raises horizontal-vertical organizational integration (including systems partnering with Big Tech, Big Insurance, academics, governments, private industry, community organizations, etc.) to the power of technical integration and moral integration. By networking the technical AI integration (of systems' data architecture linking the different stakeholders in the digital healthcare ecosystem in shared data collection, storage, analytics, and decisions) with moral integration (linking diverse beliefs and political-economic systems as a moral political economics model of local or moral globalism), this three-dimensional resilient integration conceptualizes, digitalization, and operationalizes the relevant external and internal dimensions of healthcare systems. By understanding the "GI" subsystem of economics and "respiratory" subsystem of politics in our conceptual analogy or framework of AI Health, we can see how these overarching societal structures get the needed energy and resources into healthcare systems to allow them to run (and run better). The following AI healthcare ethics chapter will explore the concept of moral integration and the final chapter on the learning healthcare system will make concrete how resilient integration can and already is beginning to function.

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AI + health ethics: moral interoperability and pluralism

8.1 No ethics, no Al, no healthcare

Let me tell you about two of my patients (whose identifying information has been withheld to protect them). The first was a poor African American male, had schizophrenia, missed most clinic appointments, was dropped off in the emergency department, was found to have multiorgan failure, and was expected to be dead by lunch (and the initial treatment team just kept him in an empty white room alone for 121 min). They said his advanced directive stated he would not want resuscitation, intubation, or dialysis so they called me as the hospitalist/internal medicine physician to admit him to the hospital to hospice so he could die. I rushed down to his room, read the directive, and confirmed it stated that he would not want the above life-saving treatment (but only if he had terminal chronic diseases—none of which he had). This is not to denigrate my colleagues. But it is to ask, did the providers not think his life was worth saving (or at least worth the 53 s it took to read the directive and confirm his wishes)? I quickly called his daughter (his medical power of attorney who could made decisions for him legally when he could not) and confirmed her approval to admit and dialyze him emergently. Two days later, he was back in his right mind. I weaned down his outpatient medications that had put him into acute renal failure, which had triggered his multiorgan failure in the first place. And his daughter wept at his bedside when she heard he was going to live. My second patient was a wealthy Caucasian female over 90 years of age, had been bedbound for over a year with end-stage dementia and heart failure, was for the last 2 weeks refusing to eat, and was brought to the hospital because she was more confused and breathing harder than usual according to her family. I confirmed she was in irreversible multiorgan failure, and sadly I had to recommend hospice to the family (echoing the cardiologist, nephrologist, and gastroenterologist who all recommended the same). But they refused. She continued to decline, was placed on a ventilator, had increasing intravenous medications maxed out to keep her blood pressure from bottoming out, and after 12 days of steady decline, went into cardiac arrest that 45 min of chest compressions and emergency medications could not reverse, until the family over the phone said to stop. So she died in the middle of the night, away from her loved ones, in a strange place, with strangers beating on her chest and breaking ribs in a futile attempt to restart a heart that had already given up.

Biology can tell us as physicians how to treat sick organs. AI can show us how to do it more efficiently. But they do not tell us how to care for the patient. I can do something is not the same as I should do something (or not do it). We have already explored how AI is rapidly transforming healthcare, particularly making it more rapid, effective, and profitable—but does this actually make real people better and happier? Politics and economics already dominate much of healthcare systems—but does this mean they are fair, particularly for poor, immigrant, and disabled patients? If ethics is simply a marketing or regulatory trick to get consumers to consume more healthcare and avoid legal attacks, it is unclear how sufficient and sustainable public trust, support, and embrace of AI-enabled healthcare can occur.

This chapter explores AI-enabled healthcare systems from an ethical standpoint to consider what is ethics, AI healthcare ethics, and practical solutions to making AI-enabled healthcare more human and equitable, not just more effective and efficient. To make it more personal and just, not just more automated and profitable. We will consider a brief overview of the theoretical foundation of ethics, current advances in their application to AI in healthcare, and concrete examples of how this process can be sustainably integrated with current and emerging system operations to maximize individual and societal outcomes, satisfaction, and well-being (not just health and financial metrics). As the clinical formulation of our AI Health model introduced, ethics can be likened to the endocrinology subsystem of the future's optimized healthcare system. Our brain's hypothalamus is the neural control system that hierarchically directs our pituitary, thyroid, adrenal glands, pancreas, testes, and ovaries to release hormones into our blood to regulate our different organs through feedback loops (catalyzing and inhibiting their functions to remain within safe limits). Similarly, good healthcare AI ethics can help orientate the various components and stakeholders within healthcare systems and the ecosystem to align (and realign when breakdown occurs) toward the common good (particularly in the health dimension) that systems are created to achieve—a unifying vision of their ultimate end or purpose which is delivering good healthcare to all patients effectively, efficiently, and equitably. Higher than grand strategy and more imminent than daily operations, good individual actions generating good collective actions toward this ultimate good of systems require good ethics on what AI-enabled healthcare should be (and practically how to correct it when it is not). Ancient education across diverse cultures and ages understood that before a healer could reason specifically from symptoms to diagnosis to treatment in the healing arts to help the sick, she/he had to understand how to essentially reason rightly. Good healthcare systems need good medicine, data science, political economics, and so on. But more fundamentally, they may need the academic philosophical discipline of

ethics and its more foundational discipline of metaphysics that shows us how to understand reality and thus reason in the first place. To provide good care to the patient by first understanding who the patient is as a person (and thus what is the good owed to them). To know that we know what we know (and how and why we know it). The central argument for this chapter is that if there is no logically valid, experientially confirmed, and multiculturally defensible global ethics in AI-enabled healthcare in our pluralistic world, there can be no healthcare nor AI. The applied argument in this chapter is how we can engineer such an ethics.

8.2 Logical, existential, and societal "suicide?" practical case for AI healthcare ethics

Following the horror of WWII and the Holocaust, 51 nations from every populated continent joined in 1945 to form the United Nations, ratifying the Universal Declaration of Human Rights (UDHR) 3 years later as its institutional DNA, foundational document, and global conviction that the "recognition of the inherent dignity and of the equal and inalienable rights of all members of the human family is the foundation of freedom, justice and peace in the world" (UN, 2022; Monlezun, 2022, 2020). On this bedrock was built modern international law, the globalized and digitalized political economic capitalist structure, and the contemporary UN and related global institutions joining the world's countries since. At the document's core is an application for our day of an ancient argument from Plato and Aristotle (echoed by leading Buddhist, Christian, Confucian, Islamic, Jewish, and early modern Enlightenment secular thinkers since)—if there is no morality then there is no humanity nor human society (and to apply to our focus here, there can thus be no healthcare nor AI). If there is no truth (objective and substantive rather than semantic and superficial), there can only be power to govern civilization (and thus the continual power struggles that halt sustained economic growth required for political stability). If there is nothing truly right, there can only be might to resolve disagreements and rule. As the last chapter explored, the political economic suprastructure of the global human society is necessarily supported by the moral substructure that entails the minimum set of common values and principles uniting people about what constitutes the common good and criteria for good or moral actions within the human community that sustain it. And such values and principles fundamentally express the belief about the deepest questions: Who am I as a human being? How are you? How can we be "we?"

Classical philosophyl describes such foundational beliefs or first principles as metaphysics or the study of being itself. The object or good studied in biology is the living organism. Data science focuses on insights generated from digital information. But in the hierarchy of human knowledge, there must be a more foundational science or discipline for not just different types of beings, objects, or goods, but for Being Itself. The physician-philosopher, Aristotle, developed metaphysics (and formal logic as a way to reason from premises to conclusions) in the fourth century B.C. to ask and answer these big questions, and thus answer the day-to-day questions. He reasoned that if he could understand (and prove) what is the essence of Being Itself or the Supreme Good, then he could understand what things essentially are (from good medicine, i.e., healing, to good politics, i.e., justice, to good mathematics, i.e., provable models). Pluralist thinkers following him worked out how to understand this hierarchy of reality (of being or the good which is convertible, as all beings exist in different modes according to their essence [what something is] and existence [that something is] according to Aristotle). To have a peaceful society, it must first be just (or ordered rightly according to this hierarchy orientated ultimately to the Good). This objective or rationally known reality is subjectively or experientially known. And so the essence of being human (i.e., humanity or human nature) once known then allows the understanding of a particular human being who exists. And thus what are the unique and common features of each human being (who exist distinctly as persons) allow us to understand what we owe to each other as we exist as social, embodied, interdependent members of a human community (Snead, 2020). The kinds of laws, companies, institutions, AI, and healthcare systems we create express and manifest our foundational beliefs of reality. For human coexistence to occur, we have to understand what human existence means. For AI to exist, we have to understand what is human intelligence not just "artificial" intelligence (and so what wisdom is or knowledge of the good). For healthcare systems to exist, we have to understand what health is (and thus what is good biological functioning of the human person).

But unique in human history, much of our modern globalized world generally tries to keep two mutually exclusive beliefs (whose tension produces much of our current challenges particularly in healthcare): there are objective truths, and there are no objective truths. As the political economics chapter introduced, our societies are practically dominated by the legacy of the 17th century Western Enlightenment (which took pieces of Aristotelianism in its Thomistic Christian formulation to create modern accounts of science, democracy, capitalism, and rights). It is difficult to find any mass consensus that the scientific method and human rights are an illusion. The vast majority of our world (and our species dating as far back as history goes) believe in the basic intelligibility of our reality or universe. We can understand at least in part how reality works through observation and reason toward cause and effects—and thus how human society should work. If reality did not operate according to gradually knowable principles, then there would be nothing essentially stopping your chair from spontaneously turning into a unicorn. And yet much of our contemporary world simultaneously assert there are no objective truths (when it typically is referring to moral truths). We can define "right" and "wrong." We can create our own identities. Our own highest good.

Our own truth. That healthcare systems or payors should supposedly be able to exclude lower paying or less societally "desirable" people. And yet humanity's belief systems (including atheist and agnostic systems) when considered logically reinforce our lived experiences of the challenges such illogical conclusions create when attempted to be implemented.

Consider a healthcare system that tells patients they are just data generators for the system, sources of zeros and ones that source code is applied to, allowing providers and system administrators to extract as much profit from as possible. Since no system in the world says anything close to that, it suggests people at least implicitly believe healthcare is somewhere different than other economic sectors. It requires not just a political economic or scientific dimension, but also a moral dimension. "I could not stand that doctor who did not treat me as a human being" is a common complaint systems often hear. It seems that there is an objectively true way of treating a patient personally, fairly, and correctly according to their unique objective identity as a human person (not simply as a faceless instantiation of the biological species). We have previously considered how the Ukrainian healthcare system in 2022 was repeatedly bombed, assaulted, and bombarded with civilian casualties from what a majority of the world's nations allege is a genocidal invasion of Russian to eliminate not only the sovereignty but also the existence of the Ukrainian people. It seems there is an objectively true way that patients and providers in healthcare systems should be treated. To put it in a more concrete way, there is no historical evidence of any physician in the world being allowed to practice without consequences after being publicly exposed as repeatedly sexually assaulting his female patients (or demonstrating gross repeated medical negligence and incompetence killing multiple patients after denying there are such truths as biology dictating what is the proper way to treat a sick person). It seems subjective feelings or positions are superseded by objective truths and standards.

It appears logically, experientially, and practically that we cannot live without being in community nor without basic rules required for our coexistence, corresponding to the actual reality of our existence. Rejecting such a metaphysical and derivative moral foundation seems to fatally doom the political economic structure it is anchored upon. Different cultures may manifest different collective pursuits and understanding of the good and reality, but this does not logically indicate there is no good or reality that is pursued. To design, create, and adapt the future's AI-enabled healthcare systems, there may be a practical need to recognize the possible consequences of rejecting a defensible moral foundation of the global human family (Harari, 2017; Monlezun, 2022):

(a) "Logical suicide" can result from the invalid method and logical contradiction of asserting there are no objective moral truths or values. As Aristotle described foundational the metaphysical "Law of Noncontradiction," two contradictory statements cannot both be true at the same time and in the same way. No logic, science, or communication can exist without this understanding. To (objectively) assert there is no objective truth is to defeat one's conclusions by attempting to make it. To generalize it is to undermine the existence of any science or technology, which depends upon this foundational metaphysical principle that allows our reason to logically progress from empirical observations about reality to generalizable principles of cause and effect and thus back to those observations (allowing us to understand our intelligible reality and act upon it to achieve desired ends through knowledge of such scientific truths).

- (b) "Existential suicide" can result from the rejection of metaphysics and its derivative objective truths, including ethics, as the uniqueness of each individual human being would be eliminated. Nietzsche argued we are essentially the will to power. Rawls said we are essentially rational, pluralist, choosing agents. Havari argued we are essentially self-made gods who can create AI "life" that can evolve even beyond ourselves (like a digital Nietzschean Superman). Yet all dominant modern accounts in this post-Enlightenment tradition dominating modern ethics and morality extinguish the difference between persons by in various forms and degrees rejecting essential (realist) metaphysical human nature (the below section on the Personalist Social Contract will define this further). If all I am is a disembodied will that choses or seeks to dominate other entities, there is nothing that essentially distinguishes me from another will or dominating force. There can be two identical cars. But not two identical persons (and thus patients) as each human being can be logically confirmed to have a unique human existence with common human nature (in Aristotle's language). There is an existential difference the world's people, nations, and belief systems universally assert between a person and an algorithm.
- (c) "Societal suicide" can result from metaphysical rejection of reality and thus morality. If there are no objective moral values, then there is no stable human society for we cannot function without shared rules of behavior (generated by a stable, sustainable, and objective third-party standard by which disputes and disagreements can be resolved). Additionally, there is growing postcolonial resistance to what is seen as a Western imperial and ideological imposition on the world's diverse belief systems of its post-Enlightenment dominant belief system (humanist scientism), undergirding its 20th century political economic manifestation of the US-led liberal capitalism (LeDrew, 2015; Muthu, 2003). What began as Western Enlightenment thinkers advocated individual freedom of belief and expression from Christianity in the 1600s became by the 1900s an identifiable, organized, ideological, secular belief system marked by scientism (asserting science trumps philosophy or other branches of human

knowledge as the only reliable means of any objective truth) and humanism (believing in the relentless Darwinian social progress of leveraging science for social justice and equity). This is not to deny the many advances and advantages generated by the Enlightenment, but it is to question its potential excesses. Critics argue that the emergence of this secular Western Enlightenment belief system informed, reinforced, and "justified" the European and later American imperialism of the early modern era, since "noncivilized" people "had" to be persuaded (or coerced) to adopt their ideological, cultural, political, and economic ideals, instruments, and institutions if they were to be allowed to participate in the "modern" world that was being manufactured by the West (though there was an influential camp of Enlightenment thinkers who argued against such colonial translation of such ideals, yet they were the minority voice). The early modern imperial age gave way to the 20th century's ideological wars and now the growing 21st century's polarization and globalization in which disputes are resolved principally by power rather than truth (as an objective third-party standard by which diverse belief systems could have a common moral language to reason together toward shared conclusions). This is not to say that reason can always resolve disagreements, but rather that power cannot be the sole means. If a patient sues a physician because she/he believes harm was done, then the suit could be tried in a court of (political) law. But if the judge and jury are corrupt, even a negligent physician could be found innocent. There practically must be a standard to which even the powerful must answer (even if not consistently) that constrains their power. Confucius in the sixth century B.C. argued (as far as we can determine) that even the ancient Chinese emperors were subordinate to the "Mandate" (命/ming) of "Heaven" (天/tiān) to rule justly, wisely, and virtuously in accord with the natural moral order. Aguinas in the 13th century following Aristotle argued similarly that people, including the powerful, naturally know and are essentially bound by the self-evident moral law to do good and avoid evil. In the 20th century, Confucian Chang and Thomistic Malik were the two primary intellectual giants who drafted the UDHR as this shared moral foundation (expressed in their different but convergent models of articulation) which argued, in the global shadow of the seeming nearannihilation and nuclear-armed total warfare of WWII, that human society destroys itself when it rejects the right and necessarily resorts to might only to resolve disputes (yet there is a growing trend in the 21st century to regard "rights" as semantics veiling power grabs rather than objectively and rationally answering and convincing what is due to each other and how to achieve it appropriately). In our technologically advanced world (increasingly threatened by the force multiplying effects of disruptive and even rogue AI, nuclear war, climate change, and pandemics), that "might" approaches an unprecedented degree of power and decentralization,

permitting fewer actors greater destructive force. Citing Russia's invasion of Ukraine (with the Russian President Putin's repeated threats of nuclear weapons), the UN Secretary-General in 2022 issued a stark warning reflecting such:

Geopolitical tensions are reaching new highs. Competition is trumping cooperation and collaboration. Distrust has replaced dialogue and disunity has replaced disarmament ... humanity is just one misunderstanding, one miscalculation away from nuclear annihilation.

8.3 Postcolonial globalization of AI healthcare ethics

8.3.1 Early global standard setting

How has the digital healthcare ecosystem sought to cooperatively calculate what good AI healthcare ethics is (for the survival of humanity and the thriving of healthcare systems)? As the PubHealth chapter introduced, a growing critical mass of diverse states, sectors, actors, and belief systems are formulating what "ethical AI" should be to respond more effectively to the societal challenges the COVID-19 pandemic laid bare. How do you empower stakeholders with vastly different degrees of "power" or political economic influence on societies to each have a more fair seat at the dialogue table where decisions are made about how societies and healthcare systems are run? How do you do so in a way that avoids the neocolonialism of institutionalized exploitation of the weaker by the stronger (including with the long shadow of post-Enlightenment European colonialism)? How do you do so especially when the AI technology increasingly driving the Fourth Industrial Revolution (that is widening the gap between richer and poorer countries) are made in the traditionally more powerful nations? We have previously considered how the 2020 Rome Call for AI Ethics proposed the first coordinated cross-sector global standard for AI ethics in the form of the Rome Principles of responsibility, transparency, impartiality, inclusion, reliability, and security/privacy (generated by international dialogue and facilitated by the UN's FAO, Big Tech, government, and the world's belief systems invited and coordinated by the Catholic Church's Vatican City) (FAO, 2020; Vatican, 2020). The Rome Call explicitly quoted the UDHR with its pluralistic framework-based Thomistic Aristotelian ethics to argue for ethical healthcare AI that serves the entire global "human family" by respecting the fundamental metaphysical principle of human "dignity and rights," flowing from objective human nature that makes everyone "free and equal ... with reason and conscience" binding all human beings to act justly to all others "in a spirit of fellowship" (Vatican et al., 2020). The subsequent EU and US DoD 2020 frameworks echoed the Rome Principles, with the 2021 WHO and UNESCO reports providing more detailed approaches to operationalizing them (including their regulatory and legal application) (EU, 2020; DoD, 2020; WHO, 2021; UNESCO, 2021).

8.3.2 WHO codification of global AI ethics standards

The WHO report in particular produced an AI healthcare ethics model that appears to increasingly be the primary template for subsequent international, national, and healthcare system frameworks (as the WHO remains the single most prominent and influential health body over the last century, acting as the UN agency leading international PubHealth efforts, including their empowerment and networking with national and local healthcare systems within a larger Sustainable Development Goals [SDG] structure) (CFR, 2022; WHO 2021). Its 2021 report explicitly argues that the net global benefits of AI healthcare can only be realized when "at the heart of its design, deployment, and use" is a human rights-based ethics approach (within the UN's political economic framework of liberal democracy following the UDHR). And similar to the UDHR, the WHO AI ethical standard is practically meant to maximize adaptability, operationalization, and anchoring within diverse belief systems, states, and healthcare systems (in contrast to a more 20th century imperial imposition). This ethics framework is contextualized strategically in the WHO's "Triple Billion" aims since 2019 for healthcare systems: promotion of UHC, protection from health emergencies (particularly pandemics), and improved well-being for 1 billion people internationally. The AI ethics framework is also contextualized operationally in the WHO's primary activities of global coordination and standard setting, as evidenced by their leadership of system-led efforts by 1980 eradicating smallpox and its 1969 implementation (with 2005 revision) of the International Health Regulations (IHR). Particularly relevant for global healthcare standard setting in AI ethics, the IHR is a legally binding international law-based agreement among the 196 nations defining nations' rights and duties in reporting and managing responses to pandemics and other international health crises. It empowers the WHO as the designated global surveillance system and lead coordinator of such efforts combating global PubHealth emergencies. Given the numerous critiques the world over we have considered alleging how the COVID-19 pandemic demonstrated the local, state, and international failures of the global healthcare community, it appears increasingly likely there will be continued push for the WHO to continue parallel development of AI-accelerated global PubHealth capacities and their ethical design and governance (as with the WHO Hub for Pandemic and Epidemic Intelligence introduced in the PubHealth chapter).

In terms of the WHO principles content, they echo but also elaborate on the Rome Principles to optimize AI benefits (to patients in healthcare systems while minimizing their risks):

(a) autonomy or impartiality (human actors remain in control of sensitive system designs and governance, both organizationally and medically, while its augmenting AI reliably operates impartially in defined parameters honoring legally defined protections for patients equally);

- (b) safety or security/privacy (AI remains compliant with quality and security standards both as algorithms and as augmenting means of healthcare delivery to protect patients, their sensitive information, and their confidentiality);
- (c) transparency (AI operates with consistent and broad explainability and intelligibility to diverse audiences for sufficiently substantive public debate and consensus on its design and governance);
- (d) responsibility (appropriately trained AI engineers and scientists remain accountable for their algorithms' consistently sufficient performance within accepted guardrails for prevention, mitigation, and redress of their unintended harms);
- (e) inclusion (algorithms avoid exclusion of disproportionate harm or underperformance for any patient population according to sociodemographic, lifestyle, or any other factors in violation of consensus-based human rights codes); and
- (f) sustainability (algorithms reliably and adaptively perform according to their consensus-based design and refinement that maximizes population net benefit and minimizes its net harm [including for the environment, energy efficiency, and job security, particularly for those prone to job loss through automation]).

8.4 International moral interoperability: superficial vague principles to substantive pluralistic cooperation

8.4.1 Data interoperability to moral interoperability

Achieving agreement on these principles across diverse stakeholders and states is an obvious success, but it does not guarantee successful translation into actually doing healthcare AI ethically and consistently. The sustainability and effectiveness of such early standard setting in AI healthcare ethics is largely shaped by its overarching global political economic structure (which multiple critiques we have already considered note is a critical barrier or enabler of ethical AI). Building on the previous chapter on this topic, we need to better detail the interface of ethics and political economics by better understanding a more nuanced and practical approach to this global ecosystem. Drawing on our healthcare AI overview chapter's highlighting data interoperability, a minimum breadth and depth of moral interoperability is required for a successful strategic architecture of a global ecosystem (integrating ethics with [while generating and animating] political economics that links diverse actors with diverse political economic models [at the international, national, and healthcare system levels] to deliver AI-enabled healthcare in our globalized world). Different stakeholders in the digital healthcare ecosystem need a minimum degree of data interoperability (allowing their varied datasets to be retrieved,

processed, stored, analyzed, and reported) so their data can "talk" to and understand each other, thereby supporting the overall strategic vision of delivering value-based healthcare collaboratively (Siwicki, 2021; Brooks-LaSure, 2021; HL7, 2022). This interoperability typically consists of semantic and syntactic interoperability. Data exchange is facilitated by the former standardizing data language and the latter by standardizing its format. If you only speak Chinese and English, and I only speak Spanish and English, then we can both communicate with each other using the standard language of English with its standard format (i.e., sentence structure of nouns, verbs, pronouns, adjectives, etc.).

The 21st Century Cures Act final rules through the US HHS's Office of the National Coordinator for Health Information and the Interoperability and Patient Access final rule through CMS promote and (in some particular contexts) mandate standard technical infrastructure and APIs for health information exchange across patients, providers (through clinics, hospitals, and public health agencies), payors, and regulatory bodies (including government agencies)—saving an estimated \$78 billion annually while improving care through more efficient data exchange (Siwicki, 2021; Brooks-LaSure, 2021; HL7, 2022). Together, they require the use of the Fast Healthcare Interoperability Resources (FHIR) international data framework (standardizing data formats, resources, or elements and APIs) for exchanging EHR data, including its computable knowledge artifacts (specified digital structures communicating healthcare data, i.e., EBM or evidence-based medicine on FHIR), digital measures (like the eCQM or electronic clinical quality measure), and clinical practice guidelines (CPGs). And together, such measures provide influential national and international standards in data interoperability (particularly the United States Core Data for Interoperability [UCSDI] to generate "data liquidity at scale") (Siwicki, 2021). These collective advances increasingly allow data securely and efficiently to flow through a digital healthcare ecosystem encompassing healthcare systems and its necessary partners to deliver value-based healthcare by real-time and relevant healthcare data generated, shared, and acted upon by diverse stakeholders.

Is there moral interoperability equivalent of the above? Strategically, data interoperability seeks to organizationally and technically align diverse actors and leverage their unique strengths to achieve the ultimate end or good of value-based healthcare equally for all patients. Operationally, it standardizes the "terms" and structure of diverse actors' diverse data so everyone can "speak" and "understand" the same data language. Yet such data science is a tool, like a sharp object that can be used as a knife to harm or scalpel to heal. The intended goal of its users, communicated to others collaboratively in the proper context, determines what it ultimately does. Dating back to at least Aristotle, ethics uniquely (and formally as an applied branch of philosophy) can identify and justify the defensible underlying intentions, goal, context, and

8.4.2 Healthcare moral interoperability in multidimensional world orders

In the final section, we will consider the substance by which this moral interoperability in healthcare may consist. But we need to briefly refine our understanding of political economics that supports or strains such interoperability (at [a] structural, [b] societal, and [c] historical levels).

(a) The prior political economics chapter considered the shifting world order framing modern healthcare as value blocks of more democratic versus more centralized capitalist states which are increasingly ideologically divided or at least distinguished. But a more precise description may rather be one of a multipolar and multidimensional international order or ecosystem consisting of overlapping networks of orders: security, economic, ideological, and digital (Bremmer, 2020, 2022). As the political economic chapter introduced, the post-WWII US facilitated an eventual digital globalization and capitalization of the world by using its international military apparatus and institutions to protect and promote free trade and liberal democratic values (where the world's richest, wealthiest, and

healthiest nations eventually dominated global affairs and this political economic framework). This order became a unipolar liberal world order as the United States and its allies were largely unchallenged from 1991 to 2008 following the Soviet Union's collapse, but the 2008 Great Recession accelerated the populist deglobalization process which was in turn further quickened by COVID-19 and then the 2022 Russian nationwide invasion of Ukraine. Concurrently, the multipolar world order increasingly emerged as no one nation could dominate the political economics or the agenda setting of the increasingly distinct though overlapping dimensions of the world order. From the G7-led world of the latter 20th and early 21st centuries to the post-2008 "G-Zero" world of "geopolitical recession," no nation or even small group of nations are rich or powerful enough any longer to impose an international governance framework, leading to overlapping domains of competition and cooperation. The US-led "democratic" world or "the West" may dominate a global security framework (including with the West's finance weaponization limiting access to capital markets and imposing sanctions as penalties particularly against Russia in 2022). China may increasingly compete to exert dominant economic influence. The democratic West and more autocratic East may compete for ideological influence including on the nonaligned Global South (as "pivot states" develop ties with multiple major powerful states to hedge against becoming overly reliant on any one in particular). And both the democratic world and China may vie for majority control of the AI-driven digital ecosystem. And healthcare systems are somehow meant to straddle these divides as the necessary stakeholders required to deliver care hail from each of those dimensions.

(b) Societally, the political economic strains on this moral interoperability in healthcare are particularly influenced by antiglobalism populist nationalism (Bremmer, 2018; Harari, 2018). Global ethics including on healthcare AI are challenged by the widespread societal backlash, accelerated following the 2008 Great Recession as noted above, in which globalism has since been increasingly perceived as a net loss by growing sectors of societies the world over. Regarded as one of the current era's most influential political scientists, John Mearsheimer argues provocatively that resistance to globalization stems from resistance to its progenitor, the USled post-WWII liberal international order, which allegedly was doomed to fail because it did not sufficiently address the importance of states' pervasive and persistent inclination to self-determination, national identity, and national security (Mearsheimer, 2019). His theory of "offensive realism" emphasizes the supposed reality of great powers (states with disproportionate capacity for projecting their will through military and economic means over weaker states, particularly neighbors) will naturally compete with each other in the rational objective to achieve and maintain regional hegemony (or dominance) in an anarchic world (in which there is

no unipolar police or power maintaining order through enforcing rules). The US-China current rivalry thus can be understood as a rising greater power challenging an established greater power for dominance. According to this vision, the emerging and foreseeable geopolitical world order increasingly consists of a thin international order (enabling cooperation in certain sectors) and a thick bounded order (led by the United States and China carving up the world's nations in strategic security competition that weaponizes all tools at their disposal, most crucially disruptive AI-driven digital technologies). Regardless of the explanatory theory, substantive empirical evidence demonstrates that despite democratic capitalism's unprecedented political stability, economic prosperity, and societal equity boosts (particularly manifest in the post-1991 period as noted with the UN SDGs), a globalizing world still leaves behind many feeling like losers rather than winners. A new world that has global economic AI and digitally enhanced supply chains (cutting out local jobs) and cultural diffusion (particularly of classical liberal values like freedom and open economics and borders) has triggered significant sectors of societies to believe they must fight to protect their "former" individual voices and ways of life that are being "attacked" by "globalist elites" (enjoying supposedly disproportionate benefits at the expense of the people). Such populist sentiment has supposedly been effectively channeled into angry nationalist collective action, from Trump to Brexit to Xi Jinping's Chinese decoupling from the West. Invoking a universal moral conception of a common human nature with resultant equal rights for all (like in the WHO's, 2021 healthcare AI ethics standards) can thus face significant headwinds in the face of such populist and nationalist resistance.

(c) Moral interoperability in healthcare AI ethics is finally challenged by the emerging historic inflexion point that highlights the growing global stagflation and debt crisis risks of a fragmented multipolar globalized world, as such economic weakness could light a match to the combustible structural weaknesses and societal fault lines in our contemporary world order. "Stagflation" refers to stagnant economic demand concurrently with persistently high unemployment and inflation (increases in prices with decreases in money's purchasing power) (World Bank, 2022; Roubini, 2022). The World Bank as of May 2022 projects that stagflation is "now likely" for the later 2020s, and potentially worse than its first emergence in the 1970s. Global energy shocks (with Russian oil, food, and fertilizer weaponized against the West coupled with Western attempts to rapidly reduce fossil fuel dependence by transition to renewable energy faster than they can make up the difference) are occurring in parallel with rising inflation and unemployment (as the post-COVID-19 global recession is being followed by rising nationalist protectionist policies globally, in addition to China's persistent zero-COVID policy and Western decoupling progressively halting its domestic growth and thus contribution to global

growth via manufacturing, while falling fertility rates particularly in the Global North are long-term slashing workforce and capital). Decades of loose monetary policy (low interest rates) and fiscal policies (high government deficit spending [on social programs typically outpacing tax collection]) are also colliding with climate change (disrupting food production, infrastructure, and economic activity with droughts and extreme weather events). It is harder to talk about AI ethics in healthcare when wars, famines, and polarizations are raging outside the hospital walls.

A world that has less trust, openness, and growth is thus one that treats ethics more like a luxury or distraction rather than a necessity or focus. Healthcare AI ethics in particular has faced significant barriers to widespread effective generation, formalization, and implementation as healthcare systems are struggling increasingly just to survive in a more politically divided, economically strained, and technologically disruptive world. A 2021 Pew Research study found that nearly 70% of AI leaders, researchers, and policymakers doubt AI including healthcare AI will be ethical (focused on the common or public good) (Rainie et al., 2021). Similar studies with IEEE's global AI standard setting, Stanford University's Institute for Human-Centered Artificial Intelligence, and the US National Security Commission on AI expressed shared concerns about global barriers to effective AI and healthcare AI ethics (which is principally irrelevant to the principal AI actors):

- (a) "ethical AI" lacks clear definitions, standards, formal training for practiembeddedness development tioners. and in current ΑI and implementation;
- (b) the primary business and government actors creating and deploying AI are focused on profit and social influence (or even control) rather than ethical concerns about the common good;
- (c) AI's rapid, widespread, disruptive, and growing societal influence cannot easily be directed to ethical applications (nor can their abuses be mitigated); and
- (d) US-China geopolitical competition (framing AI principally as a technopower military and economic arms race) supersedes any current or foreseeable efforts in ethical AI.

According to this critique in this multidimensional and multipolar world order, AI ethics functions more like a strategic afterthought or partially functioning brake (which can attempt unsuccessfully to slow down but not at all steer the principal direction, pace, and applications for AI). Building effective AI-enabled healthcare systems requires for them to be integrated with not only effective AI-enabled public healthcare networks but also the AIdriven digital ecosystem.

Such required data liquidity at scale requires efficient and embedded AI ethics by design since this global architecture cannot be feasibly retrofitted. AI unethical abuses in general and in healthcare are occurring globally, now. Waiting a decade to develop ethical AI standards fails to address not only current failings but also their increasing institutionalization in the digital ecosystem and digitally enabled healthcare systems. Rather than retrofitting on the backend, how can we do ethical healthcare AI by design on the frontend amid healthcare systems framed by their overarching (and often overriding) political economic structure? Like flying a plane while building and designing it, how can optimizing healthcare systems with AI ethics be integrated at the design phase for real-time operation improvements (in an iterative process from design to deployment to optimization and back to design)?

8.4.3 Resilient end-to-end integration of ethical healthcare AI

For ethical healthcare AI to work at the long-term strategic level and daily operational level, it thus may need to be effectively engineered and embedded in the initial design of healthcare systems. Integrally tied to the success of the organization, ethical AI is meant to be the minimalist guardrails to not just healthy functioning of systems but also their animating spirit or culture of the structure, informing the collective actions of their diverse stakeholders to a common vision (rather than imperial imposition). As physicians and patients, we can feel the difference walking into a hospital that believes that healthcare is a genuine service for the person versus another product for a consumer. Similar to how data architectures must be designed and deployed by their creators and users to the common strategic vision of the organization's mission (of what the organization is meant to ultimately do), an effective moral architecture for AI-enabled healthcare systems must have a certain degree of common end. Let us investigate if the classical concept of the common good as a "moral strategic end" may a successful candidate in our world's multidimensional world orders and pluralistic belief systems (undergirding our healthcare systems and the nations they sustain in their unique culturally conditioned political economic structures).

The conceptual transition from data interoperability to moral interoperability (understanding particular and potentially necessary features of optimal health-care AI) may be instructive for other key features for this effective healthcare AI by design (ultimately by substantive convergence of the digital healthcare ecosystem stakeholders): moral interoperability, moral agility, moral standardization, moral explainability, and moral efficiency. These features consider the above challenges identified by the worlds' experts to actual ethical AI, making them more than superficial principles. They are meant to be operational features of an effective and adaptable moral architecture, similar to the basic features of effective data architecture. To get to these features and their overall framework in the final section of this chapter, let us first build up to them by first considering their definition, context, and practical defense. Such features characterize a "resilient end-to-end integration" in ethical healthcare AI. We have explored in

the healthcare AI overview and political economic chapters how various players in the digital healthcare ecosystem leverage vertical and horizontal integration to gain strategic and operational advantages (typically through enhanced efficiencies and unique capacities relative to competitors). Let us term this the "organizational" dimension of integration. And we can term the "technical" dimension of integration as the AI-enabled data architecture of healthcare systems as digital healthcare ecosystems unify and leverage the stakeholders' convergent data streams, objectives, and capacities to better achieve systems' common end of value-based healthcare. This brings us to healthcare systems' "moral" integration in which the overarching organizational and technical integration layers are supported by the moral integration layer (like in political economics for societies). This final dimension refers to the transparent and substantive understanding from ethics back to epistemology (the philosophical study of knowledge or justified belief separate from simple opinion) to the foundational metaphysics (the deepest philosophical subdiscipline studying being itself as being). As the practical case for ethical AI healthcare proposed, the modern trend of metaphysical rejection or ambiguity undermines the possibility of any morality, like rejection or ignorance of biology undermines the existence and practice of medicine (as a practical subdiscipline derived and defended by the more foundational discipline of biology). And what is more fundamental to reality than even biology is physics and chemistry, and deeper than that is mathematics and logic, and finally all the way down to metaphysics. The definition and defense of an objective metaphysical account of reality that underlies the world's diverse belief systems (religiously unaffiliated and affiliated) may be prerequisite to ultimately defending a global bioethics for AI in healthcare systems as a common moral language, uniting the global digital healthcare ecosystem like its emerging global data architecture (as a network of increasingly interoperable systems and standards). Such an end-to-end integration (uniting organizational, technical, and moral dimensions) may thus empower healthcare systems with a resiliency to adapt efficiently and respond equitably to evolving challenges in healthcare delivery. The final section will explore the specific content of this proposed moral dimension.

8.5 Structural design re-engineering of moral interoperability in ethical healthcare AI for a divided and digitalized world

8.5.1 Theoretical overview of structural redesign

The structure for this end-to-end integration approach to ethical healthcare AI rests on its foundation (moral interoperability) and is framed by its pillars of moral agility, moral standardization, moral explainability, and moral efficiency. Consider a healthy and optimally functioning data architecture for an AI-enabled healthcare system. Data flows from diverse stakeholders are

collected, curated, and orchestrated as they are translated into a common data vocabulary and structure (with security parameters), which are then analyzed through seamless integration for real-time insights to drive organizational decisions, aligned with long-term strategies to achieve the ultimate end of value-based healthcare delivery (effectively, efficiently, and equitably). A template structure for an effective ethical healthcare AI contains similar key elements (not only since philosophy is the underlying discipline of the medical, data, and organizational sciences with similar conceptual structures but also such elements are already familiar to an emerging critical mass of AIenabled healthcare systems).

An effective and optimized ethical healthcare AI structure can enable the self-organization and orchestration according to the common, foundational organizing principle of human dignity (and thus communal diversity directing the balance between equality and liberty through the ethical principles of solidarity and subsidiarity). This foundational principle allows "moral data curation," restricting harmful inputs and clarifying relationships among shared concepts. Diverse belief systems are not all created equal, nor is diversity tolerance the ultimate adjudicating ethical principle of competing claims from different moral systems (as it is difficult to see a majority consensus of belief systems upholding, i.e., an individual system that asserts a key principle of violence against vulnerable populations, such as systems stripping basic PubHealth government resources from lower income racial minority communities to shunt them toward higher income racial majority communities). There pragmatically must be an objective third-party moral standard resolving competing claims or principles from systems therefore, as seen with the foundational principle of human dignity potentially serving as such a principle to "curate" the data streams or enumerated moral principles and concepts from diverse belief systems. The resulting self-organized orchestration facilitates a balance of cooperative competition among diverse healthcare systems and stakeholders in a structure of embedded security in which the persons included in such healthcare systems are prioritized and protected, and thus their data and equal moral status in so far as each patient is a person. "Seamless moral data integration" of various metaphysical or "moral data sources" can thus occur as substantive convergence consensus among various belief systems grows as the various data sources for this overarching "moral architecture" are aligned to a common end, namely the common good. Real-time analytics or efficient ethical calculation (considered in philosophy classically as prudential reasoning, or right reasoning to the right action to achieve the right aim in a given context). Such reasoning thus gives the resulting "moral model" an explainability for diverse audiences from diverse belief systems through a transparent epistemic pipeline from specific metaphysical principles (i.e., respect for individual dignity and thus collective diversity) to ethical conclusions (about the proper collective action in a concrete context of AI-enabled healthcare delivery). This allows imminent logical access to this framework

for all stakeholders who therefore share a common "moral data vocabulary" and "moral KPI" (key performance indicator), indicating how well shared reasoning and thus informed action is progressing to the shared end of the common good, manifested concretely in value-based healthcare delivery in the context of healthcare systems. Like in data liquidity, the resulting moral liquidity allows a hierarchical flow of moral reasoning from first or foundational metaphysical principles to applied ethical conclusions about consensusbased concrete actions.

8.5.2 Societal, technical, and political economic contexts

In the subsequent section, we will apply this theoretical model in healthcare practice to propose a movement from superficial principles to successful practice in ethical health AI. But first, like in any medical treatment, context is key as a successful treatment requires its use in the right patient at the right time in the right way. So we will consider our structural model of ethical healthcare AI in the modern societal context, including overlapping technical and political economic contexts. Similar to the clinical version of our Health AI model (conceptualizing the emerging components of the future's AIenabled thinking healthcare system like the various organ subsystems), our ethical AI model is meant to exist not in a vacuum but in the real world—a modern world with overlapping and interdependent dimensions of the world order, ranging from security to economic to ideological to digital layers as noted above. Similar to a home's architecture that considers the simple image of a home in its underlying complex layers (foundation, frame, electrical, plumbing, aesthetics, etc.), this multipolar world order conditions the structure of the present and future models of healthcare systems and thus their moral dimension (as the bedrock of common beliefs animating the culture of the societies in which those healthcare systems exist). But of all these overlapping dimensions of the world order, the digital is projected to increasingly be the dominant as the disruptive technological power of the AI-powered Fourth Industrial Revolution endows national and nontraditional actors with increasingly greater degrees of unpredictable, rapid, and disproportionate power (Bremmer, 2020, 2022). Consider the earlier example of Moderna's AIaccelerated R&D approach to the swift design, development, and deployment of the novel mRNA-based COVID-19 vaccine. Such disruptive technology not only enabled an unexpectedly brisk solution to this global crisis but it also triggered widening inequalities (in political economics returning faster to a prepandemic "normal") between the United States and developed nations able to access such a technological marvel and the developing nations without it.

The three primary societal challenges of AI in this world order for the foreseeable future (and likely much of this century and era) therefore include its risk of dehumanization, power diffusion, and destructive potential. Following Ian Bremmer's analysis supported by the UN Secretary General as

noted above, efficiency gains across healthcare and other economic sectors from AI risks continuing the current trends of sharpening the distinctions and widening the gaps among them of those deemed of greater versus less societal value. Progressively since at least the early 2000s, workers lose more jobs (and political voice) increasingly to the greater degree they lack the skilled knowledge-based labor prized in the digitalized global economy (as automation and robotics replace particularly more manufacturing and lower skilled jobs). Further, the prevalent top-down approach of Big Tech and China's rising competitors increasingly deploy algorithm-based approaches to boosting economic profit and/or societal influence (and even control) through targeted means of increasing human user engagement through narrow content access and emotional triggering (particularly fear and anger dividing "us" vs. "them"), notably through a negative feedback cycle that collectively accelerates digital addiction and societal polarization that dehumanizes users and particularly the "other." Aside from this mainstream business model for AI (increasingly extending into healthcare), AI's societal challenge of continuing its threat of progressively becoming "outlaw tech" due to its "leveling power." From alleged North Korea cyber hackers disrupting the British NHS for political and economic gain to Russian cyberattacks on Ukrainian civilian infrastructure including hospitals and their electrical grid, increasingly fewer and more decentralized actors can cause outsized damage on much larger traditional actors. And finally, great rising and declining traditional powers are progressively weaponizing AI, with the highest profile case being the US and Chinese government, military, and business actors in an arms race in which the deepest pockets drive the majority of the global AI agenda (by primarily furthering their own political and/or economic ends rather than the common good of the global human community). Such competition undermines the needed cooperation on such global existential threats as pandemics, climate change, and the disruptive technological effects on societal stability. These social challenges posed by AI thus echo the concerns of its experts about the viability and relevance of AI ethics noted in the previous section, particularly in healthcare where AI investments are so needed and already rapidly disrupting the global healthcare ecosystem. How can our proposed key features of an optimized ethical healthcare AI model survive and thrive in this societal context (Bremmer, 2020, 2022; Monlezun, 2022)?

(a) Moral interoperability to moral agility translates the embedded organizing principle of human dignity into adaptive responsiveness to changing contexts of moral dilemmas facing healthcare systems posed or addressed by AI. Consider a medical mission in a war-torn area of physicians from different countries, languages, and belief systems all converging on a field hospital treating civilian casualties—the medical and data sciences orchestrate and order their different medical specialties and skill sets through integrated healthcare delivery, even if they cannot understand

each other clearly. The heart beats the same regardless which language the lips speak. Moral interoperability allows diverse belief systems to operate in an integrated fashion in the digital healthcare ecosystem, which thus enables agile ethical decision-making for emerging threats and opportunities that allows consensus-based conclusions on concrete collective action to be identified, supported, performed, and revised.

- i. Philosophically, this interoperability occurs at a structural level when the polarity of two competing ideals or concepts are ordered to a common objective. Communal equality (i.e., healthcare equities) and personal liberty (patient autonomy) will continue to be competing extremes which separately undermine effective coherent strategic continuity, healthcare system operations, and effective political economic reforms—unless there is an objective third-party standard like the common good of the human community (which can balance both while helping resolve conflicting claims from each extreme in concrete contexts to the degree that such a good is identified, defined, and articulated persuasively to diverse audiences and belief systems).
- ii. Think of the double-stranded helix structure of DNA: the sugarphosphate linear backbone gives stability (holding in place) and flexibility (opening up to transcribe genetic material) to the complementary base pairs. Moral interoperability in healthcare AI ethics features the objective metaphysical truth as the backbone endowing complementary extremes with stability and flexibility to determine what Aristotle described as the "golden mean" of virtue of moral behavior (as the midpoint between excess and deficiency, like courage existing between recklessness and cowardice). Prudently managing the extremes of equality and liberty as a competitive cooperation in healthcare systems may thus require the truth of the human person (and thus how that informs the truth of the common good of the human community), engineering and embedding such a moral structure as the moral DNA describing moral interoperability, and giving rise organizationally to optimized AI-enabled healthcare systems. What we believe about reality informs what we believe is the right way for healthcare systems to operate, particularly with translating the disruptive effects of AI into equitable goods for all patients by orientating such utilization of healthcare AI toward the common good (in a way that allows moral agility solving dilemmas along the way to this destination).
- iii. Aristotle proposed that such metaphysical first principles allow us to understand Being Itself and thus Goodness Itself (and the derivative subordinates beings and goods that constitute reality). Truth of this reality becomes the guarantor of individual freedom and societal sovereignty (as the individual search for good expressed as and through human dignity manifests at the communal level as culture,

- requiring thus both respect for dignity and thus diversity). Dignity and diversity are akin to such complementary pairs like equality and liberty held in this moral DNA.
- iv. There is robust evidence in network science that our brains' neural networks help explain anthropologically our seemingly essential feature of societally networking—from politics to economics, to the pervasive sciences throughout them, the cultures underlying them, and the common morality grounding them, human societies seem to consistently exist as dense complementary extremes of decentralized networks (or simply "networks") and centralized networks (or "hierarchies") (Ferguson, 2018). In such an analysis, the excessive centralization of power in the Soviet hierarchy of its political economic structure precipitated its collapse for failing to sufficiently adapt rapidly enough to internal and external challenges in the later 20th century. And the excessive decentralization of the American network at a state and healthcare system level in the 2020s is threatening to undermine their political stability and economic viability amid rising inefficiencies and inequalities, with limited to absent unifying strategic vision at the societal level of what minimum degree of healthcare should be considered public goods (and how they should be financed and delivered). The moral DNA of metaphysics may provide this backbone stabilizing without excessively limiting the needed agility of competing extremes.
- **(b)** Moral standardization (rather than reduction) is facilitated by the moral interoperability of the rich diversity of pluralistic belief systems from the various stakeholders in the digital healthcare ecosystem. The common moral vocabulary of human rights and thus human security, derivative from the foundational embedded principle of human dignity, informs not only concrete and collective ethical AI actions but also the moral KPIs on whether healthcare systems are advancing toward or away from healthcare consistent with the dignity of their patients who are essentially unique persons with healthcare needs rather than replaceable and repeatable consumers with care demands. US and European secular, African and South American Christian, Middle East Muslim, Indian Hindu, and Chinese Buddhist majorities with their constitutive healthcare systems can agree in substance and practice on common ethical healthcare AI programs and policies, but for reasons inherent to their belief systems and cultures manifesting them. Accounts for the origin, specific moral principles, and ultimate destiny of humanity may differ from belief system to belief system, but what is common to them all is the human person (who is deserving of such substantive and sustained attempts at these systematic accounts, trying to make sense of our reality and how to live together in it justly with other persons).

- i. This moral standardization facilitates not only orchestration of diverse belief systems within globalized healthcare systems but also their integration outside these systems with the overarching political economic frameworks spanning their nations. The Lancet's Editor-in-Chief in 2022 following Russia's Ukrainian invasion argued that "human security" pragmatically must be integrated with national security through "health security" within healthcare systems locally and the UN Security Council and WHO globally (with related multinational organizations) (Horton, 2022). This draws on the UN's 2003 Commission on Human Security defining human security as the global collective actions to safeguard dignity, survival, and livelihood from its "critical pervasive threats," consisting of security threats to its prerequisite health security including poverty, inequities, infectious diseases, armed conflict, and humanitarian emergencies which drive disease, disability, and death (Ogata and Sen, 2003, pp. 97).
- ii. Moral standardization for ethical healthcare AI within healthcare systems thus translates dignity into a rights-based pluralistic rather than relativist approach to delivering value-based healthcare to populations as health security, while its political economic equivalent of human security orchestrates parallel state and multinational organization attempts to advance the societal conditions necessary for and facilitated by health security. Toward such a strategic vision, Bremmer recommends the "World Data Organization" (WDO) like the World Trade Organization for the multipolar digital world order dominating the other dimensions of the world order (Soat, 2019). The WDO in this argument could help solve the "zero-sum Cold Tech War" of AI in the great power conflict between the United States and China. Though empirically, globalization remains strong for raw materials, it is weakening for manufactured and service goods (i.e., with protectionism, reshoring, and friendshoring), and collapsing with the AI-driven Fourth Industrial Revolution dominating the highend goods like advanced semiconductors and integrated tech platforms. Since the AI arms race intensified between the United States and China in the latter 2010s, there are increasing multinational allegations that China has stollen at least trillions of dollars in intellectual property (particularly in AI and digital technologies via cyber espionage) from dozens of countries, including up to \$0.6 trillion annually from the United States alone (Whalen, 2022; Sganga, 2022; Pham, 2018).
- iii. The United States is increasingly responding with a coordinated international effort to protect states from China's cyberattacks (to protect their economies now) and China's ability to make advanced chips (to protect their societies in the near-term future from the perceived growing Chinese threats of military and economic

domination powered by such AI-enabled digital technologies). Can cooperative moral and technology standardization help put guardrails on such increasingly grave geopolitical tensions? Like the WTO was created by the US and its UN allies to manage global trade and resolve disputes in a liberal democratic-led world order, Bremmer proposes a WDO that can through global consensus create and promote AI standards, security, privacy, and international law in the increasingly data-driven global economy (and thus encompassed healthcare sector) of the foreseeable future (constraining the influence of maligned actors and promoting mutual benefit and thus political economic power of cooperative actors).

- iv. Such a WDO could codify the already initial WHO attempts at global AI ethics standardization. The former Prime Minister of Australia (who Henry Kissinger called "one of today's most thoughtful analysts of China's development"), Kevin Rudd, proposes a diplomatic equivalent of "managed strategic competition" by identifying and respecting such guardrails (particularly in digital and security competition) while deepening and applying cooperative frameworks (particularly in economics and PubHealth-driven sustainable development), thus mitigating the risk of continued growing risk of catastrophic global conflict (Rudd, 2022).
- (c) Moral explainability like AI explainability can be key at cultivating public trust through transparency at how foundational beliefs, assumptions, analyses, and decisions are done. Clear ethical and political economic inputs may be necessary features of such transparency. Moral interoperability again can facilitate the ethical component through standardization of diverse belief systems' inputs by a simple and explicit grounding of such inputs in a convergent metaphysical account of the person, and thus the common good informing how justice identifies and safeguards the rights of each patient to equitable access to value-based healthcare (in the concrete contexts of AI-enabled healthcare systems and a human security—focused multidimensional world order). But the moral explainability can also enable the traditionally unrecognized or underreported political economic calculations and influences driving much of the ethical or unethical AI use specifically in healthcare, and more generally about the ethical or unethical use of AI in general.
 - i. After initially receiving global praise for its early perceived successes curbing the impact of COVID-19, China's increasingly centralized and autocratic leadership concentrated in Xi Jinping receiving growing criticism domestically and internationally for its persistent reliance on its "zero-COVID policy" (attempting to prevent any community spread through strict and often prolonged lockdowns), including from the WHO Director-General who in 2022 called the policy not "sustainable" (Kuo, 2022; Schuman, 2022). Softer critique

questions the net benefit of hundreds of millions of people for 3 years facing the unpredictable on-and-off shuttering of factories and grocery stores which they depend on for their livelihoods and survival. The critique is heightened at a time where no nation 3 years out from the pandemic's emergence has attempted such a long-term policy that is rapidly depressing China's economy and that of the world without any clear benefit of reducing COVID deaths (when there are numerous effective vaccines available). Sharper critique asserts that this "draconian" health policy is driven not by science-informed PubHealth but nationalism-informed political power (deprioritizing health and economics by rejecting effective Western vaccines and alternative policy successes). Regardless of the rationale, comprehending the policy is incomplete without the larger societal context informing its formulation and application. Across the world for instance, understanding the booming Israeli biotechnology sector and UHC is limited without considering its context in what former Prime Minister describes as its "Iron Tringle of Peace" as a political economic framework (in which the soft power of human rights-based diplomacy is seen as futile unless backed up by the hard power of military and economic strength) (Netanyahu, 2022).

- ii. A two-dimensional understanding of an earthquake is not enough to understand what an earthquake is and how to predict the next one by just looking to the left and right of you. A three-dimensional geological view is required to understand how our planet's core supports a mantle and overlying crust layers, and thus how the mapping of the latter two (as they form tectonic plates whose collision pushing together and pulling apart causes the seismic waves we feel often catastrophically) allows us some degree of prediction and mitigation of future effects. Moral explainability may similarly allow transparent three-dimensional mapping of AI-enabled healthcare systems by understanding their moral core supporting their overarching technology-enabled political economic structures, and how those fault lines can be managed as much as possible lest they undermine efficient and equitable value-based AI healthcare.
- iii. The above noted 2022 Pew Research study of AI experts similarly emphasizes that ethical AI cannot be understood without explaining its dominant "context of late-stage capitalism" prioritizing "efficiency, scale, and automation," though a "truly ethical stance on AI requires" rather prioritizing "augmentation, localized context, and inclusion" (Rainie et al., 2021). The former centralizes data, power, and design control, while the latter can empower local agency, capacity, and self-determination of AI actors and their enabled healthcare systems.

- iv. Moral explainability of such factors help strength case for the above moral standardization push like with the WDO and related measures for strategic managed competition to leverage the collective power of diverse states, healthcare systems, and underlying belief systems to advance the successful design and deployment of ethical healthcare AI.
- v. Understanding the challenges and opportunities for globalized networks of actors who can leverage their comparative strengths for AIenabled healthcare systems thus may require not only explaining the current political economic fault lines and guardrails but also their historical trajectories. The rise and fall of the great powers of imperial Europe (and by extension its former American colony), Russia, and China shapes much of the current fault lines with the reshoring USled democratic block increasingly facing off with the uneasy alliance of a rising or even peaking China (flexing its muscles in its AI arms race with the United States) and declining Russia (arguably attempting one final time to assert regional control over Ukraine in its 2022 invasion in the fading twilight of its military and economic power) (Kaplan, 2022). The outsized global influence of the democratic security apparatus of the US and its European and Asian allies (including Japan, South Korea, and Australia), international democratic dominated financing apparatus (using the US dollar as the global reserve currency), and ideological framework (of the US-led order emphasizing rights, freedom, open borders, and free trade amid the China-Russia-Iran competitor countering with its version of more autocratic and nationalist anti-US order) underline the importance of moral explainability to take seriously this societal context of AI healthcare, and to inform pragmatically how consensus in ethical AI can occur for collective action bridging such multidimensional world orders.
- (d) Moral efficiency is the ultimate feature generated by the intermediary features of moral agility, standardization, and explainability, which cumulatively draw from the foundational feature of moral interoperability. Like AI, healthcare AI ethics ultimately must work if healthcare systems are going to be able to use them. This AI ethical efficiency operates in a healthcare system operationally like the national security approach of successfully responding to a threat by first correctly framing it: identify the nature of the problem, the inventory of the system's vital interests affected by it, the overarching strategy and related practical objectives, and the challenges and opportunities to achieve the needed ends by integrating a systems' capacities and those of aligned partners in the digital healthcare ecosystem (McMaster and Roberts, 2022). The primary global challenges to effective AI ethics identified by the above Pew Research 2022 study (standardization, relevance, speed, and strategy) are addressed

in this moral efficiency feature beginning with a "trustworthy deep learning AI co-design"—like approach (introduced in the AI healthcare overview chapter) by a cross-sector collaboration of diverse stakeholders at the initial design phase (with providers, data scientists, leaders, policymakers, legal counsel, finance officials, community members, etc.), progress to consideration of the societal, cultural, and political economic contexts of the problem and potential solutions, draw on their moral interoperability foundation (uniting stakeholders' pluralistic belief system's substantive common ground of the dignity, rights, and diversity of patient populations informing ethical calculations), and ultimately produce ethical consensus for collective AI-enabled healthcare system action. This efficiency additionally emphasizes continuous quality improvement, speed, accuracy, and precision (including incorporating elements of AI augmentation to increasingly embed such AI ethical considerations in the ambient data architecture, analysis, and decisions at the clinical and organizational levels, while still retaining sufficient human oversight, public transparency, and system accountability for healthcare systems' overall efficiency and equity).

i. This model feature of AI ethics draws on one of the world's most influential experts on public bioethics and former US chief negotiator for the UN's Universal Declaration on Bioethics and Human Rights (UDBHR), O. Carter Snead, who argued in his 2020 Harvard University Press book integrating modern legal theory with Aristotelian metaphysics that we are fundamentally embodied dependent rational animals (Snead, 2020). Biologically, our natural limits require us to depend on the care and support of others from our earliest to final moments (especially children, the sick, disabled, and elderly who are the most vulnerable) in a way that is not sufficiently explained by the prevalent modern anthropological view (that we are simply Darwinian material beings self-interestedly seeking to optimize our own survival), nor is it explained by the dominant post-European Enlightenment classical liberal legal view (that we are primarily disembodied autonomous wills whose greatest good is realized in the unrestrained or minimally restrained assertion of subjective and shifting preferences). Snead in contrast avoids the typical conservative-liberal or religious-secular ideological framing and instead emphasizes embodiment and dependence in a way that he argues is more metaphysically and logically accurate, experientially validated, and pragmatically efficient in deriving ethical consensus in a pluralistic modern world (that is nonetheless inhabited by unique human persons with a common human nature fulfilled in the care of others in the common good, through which our individual flourishing and happiness is realized). Ethics is the systematic understanding of how to treat other persons by the derivative metaphysics defining who

- persons first are and thus what is owed to them, with the derivative legal framework assigns minimum standards for such just treatment.
- ii. AI's technical simplification of patients to zero's and one's requires a proportionate and shared metaphysical recovery of the patient who is first a person to protect the moral clarify of the existential division between man and machine, and ultimately the unique person versus nameless consumer or good (as the good or dignity of each person is not reducible due to arbitrary classifications or unequal societal respect or healthcare system treatment). Moral efficiency requires such metaphysical clarity in this AI ethical model's grounding in such moral interoperability.
- iii. Medicine, math, and political economics are insufficient for sustainable healthcare system operations and equity in and of themselves alone. Healthcare is team sport, predicated on the preexisting human community bound by common values, beliefs, and goals. As such, it is a microcosm and manifestation of society. Rather than profit or power, the sustainable society and thus its constitutive AI-enabled healthcare systems runs on justice (which is the object and essence of ethics). Medicine, math, and political economics cannot with their knowledge domains or technical methodologies sufficiently identify or sketch the steps needed to advance toward justice let alone secure the minimum social arrangements required to allow the functioning of the system in and of themselves. Economic growth and political stability are ultimately undermined when equity is unjustly compromised, and this population equity requires the proper orientation of individual freedom to the common destination of the common good (which multicultural metaphysics helps identify and ethics helps advance toward).
- iv. Not all that is ethical is legal and not all that is legal is ethical. Individual conscience requires moral education and reformation with legal codification of a minimum shared societal standard of right behavior toward others. Society and healthcare systems ultimately depend on efficient AI ethics to facilitate the healthy functioning of each of the above components and their right relationship (and reengineering and reconciliation as needed).
- v. Efficient healthcare ultimately requires the shared foundational knowledge of biology and mathematics-informed medical and data sciences, a knowledge that is standardized across providers who can agilely respond to changing situations for the system and its patients, but also explain their shared reasoning to arrive at consensus-based collective clinical and organizational action. Efficient AI ethics for systems appears to require similar features.

8.6 Applied healthcare AI ethics: AiCE + Personalist Social Contract

8.6.1 AI ethics: technical to global public health

Now that we have considered theoretically how an optimized AI healthcare ethics may look like and its societal context, let us move on to the final two considerations of this chapter about the current and emerging states of AI ethics in healthcare. A 2022 scoping review of AI healthcare ethics assessing 12.722 articles demonstrated that the bulk of this research has focused on the domains of PrMed, diagnostics, and robotics in addition to the ethical concerns of trust, privacy, responsibility, and bias (Murphy et al., 2021). Notably underrepresented or even absent was consideration of the domains of AI ethics of PopHealth, PubHealth, and global PubHealth and the ethical concerns in lowand middle-income countries. There is not only ethical urgency to reduce inequities by at least featuring dual focus on high- in addition to low- and middle-income countries but also greater technical potential and system profitability by dual focus on PrMed and PubHealth (given the greater societal benefit, amount of data, and existing system technical and financial inefficiencies for the latter vs. the former). Though gradual and overshadowed by the geopolitical conflict-based world order (notably with the United States and China), we have already seen the above examples of growing institutional, academic, and public awareness and promotion of a more equitable (for higher and lower income communities) and system-based approach (PrMed and PubHealth) to AI and its ethics from improved digital literacy and connectivity, healthcare system digitalizing, integration of PrMed and PubHealth (including via PopHealth), global pandemic early warning systems, telehealth bridging the above, and value blocks of nations in parallel with international institutions like the WHO (and potentially even some version of the WDO) facilitating AI ethics standardization and resource coordination through centers of excellence and multinational knowledge and capacity-sharing networks.

8.6.2 Embedded AI ethics by design versus retrofitting the global data architecture

Concurrent with the macro trends in AI ethics from single individual focus to dual or integrated population focus, the micro trends in AI ethics manifest growing attempts to integrate the theoretical and technical aspects of AI. Stuart McLennan and the Technical University of Munich's Embedded Ethics Lab have helped pioneer embedded AI ethics to transition from the dominant approach in AI ethics (enumeration of and consensus on high-level principles) to their practical application (uniting data scientists and engineers developing AI with the ethicists, clinicians, patient advocates, policymakers, system

leaders, and industry representatives to "anticipate, identify, and address" ethical challenges of AI technologies in their end-to-end design to deployment to optimization in an iterative continuous quality cycle) (McLennan et al., 2022). This collaborative, multidisciplinary, and cross-sector approach facilitates a more comprehensive, accurate, precise, and practical understanding of the technical, ethical, policy, and social implications of AI technologies—with a particular emphasis on societal equity not simply technical efficiency—to help prevent rather than simply fix significant and pervasive challenges to healthcare AI once it is already deployed (and increasingly too entrenched to meaningfully address). Early critique of this embedded approach highlights its greater institutional, financial, and time investment (rather than the current approach typically of data scientists deploying healthcare AI often with vague understanding of what system leaders and clinicians actually need, or the population concerns for their inequity and unethical impact). Proponents point out that building a house right the first time is often far safer, cheaper, and faster than having to retrofit or even rebuild a rushed product with prohibitively numerous and pervasive design and structural weaknesses. This debate takes on an even more serious and challenging question when it is extrapolated to the emerging global data architecture for the global digital healthcare ecosystem—if we continue to supposedly rush AI into healthcare, will it be too difficult to retrofit or reengineer the whole of it when its related complications become increasingly clear and costly, worsening healthcare system efficiencies and inequities? Can defensible and efficient AI ethics be engineered into the global ecosystem in a way that allows augmentation and even some degree of automation to increase its ROI and societal trust in it?

8.6.3 AiCE + Personalist Social Contract = resilient, global, pluralist, and practical AI ethics by design

So let us investigate a candidate for a resilient, reliable, trustworthy, efficient, and still practical AI healthcare ethics that is designed to facilitate consensus while increasing efficiency through embedded, augmented, and automated ethics in healthcare systems' clinical and organizational operations in a globalized, digitalized, and pluralistic international human community of multidimensional and multipolar world order: AiCE. Introduced in the Pub-Health chapter, this "AI-driven computational ethical and policy analysis" or AiCE seeks to translate the WHO AI ethical high-level principles into the reality of healthcare systems within an end-to-end resilient (moral, organizational, and technical) framework. It additionally is designed to respond to the Pew Research AI experts' concerns about it being sufficiently standardized (across pluralistic stakeholders through its moral interoperability), relevant and rapid (through its embedded design feature), and strategic (deliberately positioned to balance the competition and cooperation demands of the multidimensional world order).

Its strategic defense runs as follows. AI is already out of the gate, rapidly transforming healthcare in a digitalized and globalized world, which is nonetheless increasingly divided between great power competition weaponizing AI in an arms race which undermines the necessary global cooperation on shared existential threats (including worsening inequalities and related political instability from disruptive AI technologies, pandemics, nuclear war, etc.). It is too difficult and costly to retrofit the global data architecture underlying the digital world order (progressively dominating the other dimensions of the world order including security, economic, etc.) that shapes the digital healthcare ecosystems and its constitutive healthcare systems. Substantive, pluralistic, and practical AI ethics are needed now that can run iteratively and concurrently with existing AI healthcare that increasingly aligns its stakeholders with a common defensible strategic end, like the common good essentially, manifested societally as justice (giving to each what is due them as members of the global human family) and in healthcare as equitable value-based healthcare. Though the top-performing healthcare systems appear to be in AI-enabled social welfare capitalist democracies, they are becoming more unaffordable especially amid the progressive likelihood of deglobalization stagflation. It appears that an enhanced dual focus not only on acute, demand-based, PrMed-driven healthcare but also on preventive, PopHealth-based, global PubHealth-driven healthcare is required through a pragmatic local globalism approach prioritizing local needs without sacrificing necessary cooperation for regional, national, and international collaboration with the rest of the digital healthcare ecosystem. The tensions of the above paired extremes or opposites in a world of diverse states, healthcare systems, and belief systems may be united from *inside* rather than imposed from *outside* these communities by drawing on our shared essential and existential reality as unique members of the common human family. Certain minimum features of shared understanding of our human reality, dignity, rights, duties, individual flourishing, and common good are already foundationally embedded and imminent in our world's diverse cultures and belief systems, in addition to being historically codified in the world's largest political organization (the UN), shared moral standard (the human dignity and rights-based UDHR), and modern international law (derivative explicitly from the UDHR). Within AiCE, the Personalist Social Contact (PSC) introduced in the PubHealth chapter uniquely defines, describes, and translates the above argument concretely into global healthcare AI ethics (critical for the political stability, economic prosperity, and cultural diversity of the world's healthcare systems) in a way that is explainable and transparent (from metaphysics to morality to pluralism) in addition to being simple, accessible, concrete, and universal by focusing on the foundational shared reality of the human person (logically, experientially, scientifically, and pluralistically considered).

Building on O. Carter Snead who built on Aristotle (what the PSC historically and philosophically argues is the philosophical foundation for the

UDHR), the PSC starts with the simple reflection on how we live and act. We naturally exist in community with others, come into existence by others, nurtured when we are most vulnerable throughout childhood, and progressively develop our capacities to flourish individually by in turn caring for the community. Within his reality of embodied and embedded vulnerability and virtue, we can see how we do not act aimlessly, but always aiming toward a perceived or true good. Good ethics is about educating progressively toward the right goods and right means of attaining them in community in a manner respecting the rights of others to attain their goods as they do ours (as we need others to achieve their good as we need them). This may appear too vague or irrelevant now so let us consider its specific content, structure, and application to AI healthcare with clinical examples.

8.6.4 Personalist Social Contract: strategy, structure, and content

Strategically as the PubHealth chapter introduced, before the 2020 Rome Call for AI Ethics published the first cross-sector global standard for AI ethics for practical application, they first advanced its theoretical foundation by recognizing the PSC as part of the world's top doctoral dissertation on AI ethics (Garcia, 2020). The above section noted how the Rome Principles were explicitly anchored by the UDHR, and the PSC details philosophically and historically its classical Thomistic Aristotelian foundation and modern social contract framework. The PSC was additionally designed to operate within the embedded, augmented, automated, and iterative design of AiCE within healthcare system operations (clinically and organizationally) and has since been deployed to optimize health equities and outcomes in cardiac arrest, COVID-19 and related pandemics, and bioterrorism and healthcare systems caught in great power-related armed conflict (Monlezun et al., 2021, 2022a, 2022b). The first step of AiCE is the clinical analysis using the novel ML integration with causal inference statistics, followed by the second step of cost-effectiveness and benefit (typically of a treatment vs. standard of care of interest). The final step is the computational ethical analysis taking its empirical inputs from the preceding steps to translate clinical and cost insights into ethical policy decisions.

The PSC was selected as the primary ethical framework in the final AiCE step for its (a) practical, (b) political, and (c) philosophical comparative advantages vs. alternatives:

(a) Practically, the PSC makes philosophically intelligible (and is historically expressed in) modernity's dominant ethical system of human dignity-based rights and duties (formally articulated in the UN's UDHR and the derivative modern international law and associated international ethical standards and conventions). Additionally, PSC is the only global (pluralistic) bioethics model which enables collaborative, cooperative

convergence of the world's religiously unaffiliated and affiliated belief systems (in alphabetical order)—Buddhism, Christianity, Confucianism, Daoism, Hinduism, Islam, Judaism, folk religions, and secularism (agnosticism and atheism)—accounting for over 99% of people globally (Hackett and Grim, 2012). On the other hand, the alternative popular post-European Enlightenment ethical frameworks of Kantian, utilitarian, social contract, and similar ethics practically exclude nearly 90% of the global population from ethical debate by ultimately imposing principles that violate their foundational principles. Approximately 9 of every 10 people on the planet identify with a religiously affiliated belief system which features a realist metaphysical foundation and derivative first principles (arguing there are objective truths which by our common human nature we have a common duty to honor, like to avoid deliberately harming innocents). Such post-Enlightenment frameworks ultimately deny or exclude such objective foundation and derivative principles (i.e., the nonhuman or divine origin of being in general and human beings in particular, with such first principles being unable to be subordinated to the modern frameworks' constructive rather than logically derivative principles, including the Kantian categorical imperatives, utilitarianism's utility principle, or Rawls' social contract as the highest ethical standards resolving disagreements among belief systems and people). The PSC bridges both religiously unaffiliated and affiliated by emphasizing the priority and reality of the human person central to both types of systems.

- (b) Politically, the PSC can uniquely facilitate the substantive convergence of the world's countries, joined in the UN explicitly grounded in the UDHR ethics since the modern human community joined following World War II to avert future world wars (given their concern about the related threat of extinction). Almost every nation on the planet is already united in the UN, humanity's largest political organization, which is built on the shared philosophical foundation of human rights and duties derivative from human dignity. This foundation and its primary principles were asserted as objective truth from the 1948 UDHR and invoked in objective substance rather than political semantics since in all subsequent conventions to the current day. The PSC provides the philosophical depth to understand the logical structure of the world's shared ethical system (which increasingly needs to be understood in its depth to resolve the growing breadth of ethical dilemmas).
- (c) Philosophically, the PSC retains the insights of modern ethical principles but anchors them in an Aristotelian-derived Thomistic Personalism (with its realist metaphysical foundation), so bypassing the metaphysical foundational weaknesses of alternative modern ethical frameworks with the subsequent logical self-contradictions and difficulty producing ethical consensus (of note, this is a big claim with the detailed supportive systematic argument found in full in Monlezun 2022). But rather than solely

utilizing this classical metaphysics, it makes it more intelligible and comprehensive by integrating it with modern pluralist and personalist insights and those from competing modern ethical systems (while post-Enlightenment systems largely reject implicitly or explicitly a knowable realist metaphysics). The PSC thus emphasizes the individuality, subjectivity, and experience of each person while still rooting and defending these features of reality in a realist metaphysics that defines and justifies such features as derivative from the communality, objectivity, and universal nature of each person. This foundation recovers the philosophical sustainability allowing logic to reach defensible and shared conclusions amid pluralistic stakeholders, conclusions which modern ethical nonrealist frameworks may struggle to reach because of an absence of metaphysical and thus moral interoperability from people of different ethical frameworks (including logically reaching such desired conclusions as protecting dignity, multiculturalism, and pluralism). The PSC enables and empowers a sustainable and substantive rather than superficial and semantic convergence of diverse belief systems by superseding the distinction of religious and nonreligious, integrating our collective pluralistic strengths and insights of modern philosophy (i.e., the pragmatic popularity of the Rawlsian social contract and intuitive utility principle) with insights from classical philosophy (i.e., with a Thomistic-Aristotelian metaphysics facilitating a more foundational consensus underlying diverse belief systems through a transcendent logical defense of the reality of the human person, universal across people and inherent within their belief systems, while still prioritizing each person's unique lived experience).

Structurally, the PSC is a novel integration of classical ethics (particularly realist-based Thomistic-Aristotelian virtue ethics, framed with a dual focus on the personalist emphasis on the structure of individual experience, and articulated by William Carlo's esse/essence revision of Norris Clarke's Strong Thomistic Personalism, themselves derivative formulations of Thomism as an integration of Aristotelianism and Platonism) and modern ethics (especially the political liberalist conception of justice as fairness by the utilitarianisminformed Rawlsian social contract, bounded by Kantian deontology, and supplemented by Marxist, feminist, deconstructionist, and ecological ethics) (Monlezun, 2022; Shaeffer, 2016; Carlo, 1966; Clarke, 1994, chapter 3; Aristotle, 2001, 323 B.C., bk. XII; Clarke, 1993, pp. 4–5; Clarke, 2009, pp. 226-227; Aquinas, 1274, I.5.1, I.29.3, Ia-IIae.61.2, IIi.58.3, I.44.4; Garcia and Monlezun, 2022, pp. 5-24).

Content-wise, the PSC in brief attempts a "robust metaphysical justification, anthropological consistency, multicultural sensitivity, pluralistic convergence, political embeddedness, economic pragmatism, and ethical clarity in its summary theoretical principles" (Monlezun et al., 2022c). This model is built on an Aristotelian realist metaphysical foundation noted above that recognizes

being as being as existing in active form only: being is "be-ing" that communicates itself to others. Yet among material beings, the human being can uniquely communicate herself/himself in a personal way through selfawareness enabling self-possession, self-gift, and reciprocal reception. This metaphysical foundation sees the person in her/his subjective and objective dimensions as a unique human being who is happiest and most complete through a personal and deliberate gift of self to other persons in love, characterizing this reciprocal gift reception orientated to the good of the other by recognizing the intrinsic good of the person. The flourishing of the person is facilitated by achieving the fullness of justice that in human relations is manifested as love individually—desiring the good of the other person as other—and communally as achieving the common good. Further, justice to other nonhuman beings is achieved in responsible care for the larger ecosystem of nonhuman beings in our common home. Such a conception argues the person is like a universe unto herself/himself with a unique identity and dignity that required being treated as such. The proper response to a patient is thus to treat her/him as a unique person as an end or good in and of herself/himself. The person can therefore never primarily be a means to a physician's end such as simply to generate profit. We know when others "see us as we are' rather than simply "using us." Accordingly, the PSC foundation highlights an extended metaphysical defense of multiculturalism that explicitly references the canonical texts and thought leaders of the world's diverse belief systems to logically map out and prove what is generally regarded as self-evident principles. It details and defends the substantive converging rather than Rawlsian-like overlapping-consensus on the metaphysical not simply political identity of the person but also the derivative insights of respect for the individual dignity (an intrinsic good), communal culture (collectively seeking the good), and the common good (encompassing what is required for the individual flourishing of each person). This three-dimensional metaphysical (or personal dimension) conception of the person having such intrinsic nonfinite value from her/his existential origin, moral order, and goodness orientation allows her/his dignity or intrinsic value (nonfinite or arbitrarily limited externally) to be understood commonly across belief systems (which upon respectful examination of them from within these systems in their own words supports this 3D conception of dignity that thus entails certain enumerated rights to be treated as such, with the correlative duty to honor such rights according to justice).

What experientially and logically follow from this first principle of being in this metaphysical foundation are the PSC's theoretical principles (respect for individual dignity and communal culture). Following Aristotle, dignity and culture are teleological, or end orientated. The intrinsic good of our dignity enables us to know, will, and act toward the good (with our individual flourishing realized in the ultimate good, manifested temporally as the common good which is achieved in our collective support of each other to reach it). Culture is the collective search for goodness, therefore entailing its respect similar to dignity (though such respect is bounded by the good, as inhuman actions like systematically excluding the poor from healthcare systems to boost their profitability or deliberately harming vulnerable people given the power differential of strong vs. weak are unjust in this ethical framework and thus should not be respected). Culture is understood as the collective, interdependent, relational, and communal search for the ultimate good or goodness itself as the most fundamental, human, and personal of all endeavors and acts.

These theoretical principles are operationalized in the PSC practical principles of subsidiarity (respecting governance at the most local level possible to organize, order, and coordinate collective actions for the individual and common good) and solidarity (respecting the rights of each person needed for her/his flourishing as members of the human family). From the practical principles flows the primary ethical principle of the Personalist Norm (elevating Kant's second categorical imperative from a minimalist constructivist Enlightenment ethical principle to the personal dimension by arguing for love as the essence and highest expression of ethics, since the "person is a good toward which the only proper and adequate attitude is love" expressed similarly in numerous belief systems as the "Golden Rule" principle below) (Wojtyla, 1993).

8.6.5 AiCE + Personalist Social Contract: pluralist application for global healthcare AI ethics

The PSC relationally orders these principles in a pluralistic social contract-based framework that is derivative from the above Aristotelian (Thomistic Personalist) metaphysical foundation by anchoring, integrating, and applying the principles and approaches of the world's diverse belief systems (with careful attention dedicated to the nuances between and among these frameworks including atheism and agnosticism) (Phramaha, 2012; Paul, 1995a,b; Tsai, 2005; Hansen, 2020; Nadkarni, 2013; Hayatli, 2009; Rothenberg, 2017; Rawls, 2005; Monlezun, 2022):

- (a) Buddhism (*sila* or virtue describes the equality of all living beings and reciprocal respect due to each other);
- (b) Christianity (equal existential dignity and rights flow from God who as Creator makes every person in His Divine Image as His children who by their free choice can be redeemed and elevated to union with God through the incarnation, death, and resurrection of Jesus Christ as God uniting flesh to His Divine nature who offers the path to this union through love open to all belief systems);
- (c) Confucianism (yi or justice and jen or humaneness express equality and reciprocal respect of others);

- (d) Daoism (to live in harmony with the way or normative natural dao ordering and honoring the diverse paths or human dao's of each person);
- (e) Hinduism (dharma or ethics normatively advances the good of others by ordering all human goals through integrating both deontological and consequentialist ethics);
- (f) Islam (the Shariah enumerates the rights that are due among fellow human beings, while sharing a similar vision of divine origin, order, and orientation of Christianity and Judaism endowing persons with unique dignity);
- (g) Judaism (the Torah's Leviticus Chapter 19 specifies the Golden Rule or "love your neighbor as yourself," flowing from the similar metaphysical conception and thus moral principles as noted with Christianity and Islam above); and
- (h) Religiously unaffiliated (articulated prominently by the Rawlsian conception of justice as fairness, Darwinian social cooperation as facilitating shared survival, and secular humanist concerns for social justice).

The PSC's pluralistic ethics in summary practically seeks to demonstrate logically, experientially, and historically that our diverse belief systems globally converge substantively, existentially, metaphysically, and morally on the shared conviction and reality of the intrinsic dignity of every human person. Regardless of any arbitrarily identified traits as sex, nationality, belief system, etc., this dignity flows from her/his biological identity as a human being, flourishes through operating according to the moral order expressed in just treatment of others in the collective action toward the human community's common good, and is perfected in what Aristotle described as knowing and becoming united with goodness itself (i.e., a good physician becomes such by progressively knowing what good medicine is until it "becomes" part of who she/he is). Accordingly, the person is a rational animal on a continual spectrum of dependent embodiment from the first to the final moment of life, requiring justice ordering moral actions within the human community for its collective survival and flourishing (collectively and individually). The PSC does not reduce or equate the various principles of diverse belief systems, and as such avoids the logical fallacies and contradictions of ethical relativism (objectively asserting there are no objective ethical systems, thus preventing any ethical conclusion from being objectively coherent and compelling). Rather, it demonstrates the structure and extent of their convergent insights in a shared reality of human existence and essence (in Aristotle's terms). The PSC further articulates how its principles can thus be applied in concrete, specific, pluralistic situations. In healthcare, it understands the patient as a person and the treating healthcare system in a societally diverse and complex network of overlapping human communities or multidimensional world orders, which can nonetheless be sustainably and substantively anchored in the starting point of the human person and orientated toward the common good (achieved in

different ways according to the different domains, incentives, limitations, and methodologies of those communities).

A 2022 example of the PSC integrated in embedded, augmented, automated, and iterative AI healthcare ethics is a nationally representative analysis of 101,521,656 hospitalizations using AiCE and EHR data to identify racial and cancer disparities in cardiac arrest (Monlezun et al., 2022a). Across low-, middle-, and high-income nations and communities, healthcare systems have not significantly, sustainably, nor equitably improved arrest outcomes in nearly 3 decades. This multicenter analysis using ML-PSr and DL algorithms on over 4000 hospitals (in low-, medium-, and high-income neighborhoods) determined African Americans, Hispanics, and Asian Americans with active cancer compared to Caucasians with active cancer were significantly less likely to receive postarrest cardiac catheterization, and that by correcting such racial disparities, nearly 100 additional lives and \$19.9 billion in net benefit annually in the United States alone could be saved, while demonstrating a novel risk stratification tool to guide early clinical decision-making for patients who are more likely to survive (and so guiding more effective, efficient, equitable, and appropriately aggressive treatment). This proof-of-concept analysis suggests that such AI-driven clinical, cost-effectiveness, and computational ethical analysis can be done and applied in real time through healthcare systems' existing EHR with justification on ethical and financial grounds for doing so.

This chapter therefore has proposed that effective, efficient, and equitable healthcare systems must not only successfully navigate their AI-driven digital transformation in the technical dimension and strategic niche in a cooperatively competitive emerging multidimensional world order in the political economic dimension but also substantively anchor their systems in the moral foundation underlying these societal frameworks emerging from it. AI requires collective action, which in turn requires common beliefs and goals uniting its related diverse stakeholders. Recovering a substantive global ethics for healthcare AI may thus be a critical and notably underinvested dimension of healthcare systems whose numerous critics globally argue fall short when they fail to see the patient first as a person. Early attempts at global standard setting for healthcare AI ethics from private-public partnerships like with the 2020 Rome Call for Ethics to the most health-focused 2021 WHO report provide important early advances in consensus on enumerated high-level principles. But to be effective, healthcare AI ethics may require a pragmatic approach seeking to embed AI ethics in the initial design process through a multidisciplinary approach uniting not only providers, patients, and payors but also data scientists, leaders, and policymakers, joined by the common goal of the common good underlying diverse states, healthcare systems, and belief systems. The PSC within the AiCE may be a candidate for such an efficient and equitable healthcare AI ethics model and methodology which already has been deployed in multiple clinical, PopHealth, and PubHealth contexts globally through existing data architectures and clinical workflows.

Regardless of the ultimate models and methodologies utilized by the emerging model of the future's AI-enabled healthcare system, it appears there is growing theoretical and empirical evidence that successful versions in our digitalized multidimensional world orders will require a moral interoperability foundation uniting our pluralistic global human community and supporting its model pillars of moral agility, moral standardization, moral explainability, and moral efficiency. Like good AI, good AI ethics may similarly need such feature of best practices in the digital domain. Moral interoperability can demonstrate substantive foundational agreement on human dignity. Moral agility emphasizes the capacity building for iterative quality improvement from the multidisciplinary design to deployment phase of healthcare AI in a way that anticipates, prevents, and resolves ethical dilemmas in rapidly changing though still predictable societal and technical contexts. Moral efficiency may empower concrete resolution of ethical dilemmas, notably through an organizational hierarchy of diverse principles in pluralistic framework, nonetheless ordered toward the common good achieved by justice (to which the foundational organizing principle of dignity points to and by which it is fulfilled). Moral standardization based on dignity may enable fundamental universal convergence of resulting standards and formal education for healthcare AI ethics, with local adaptation for context-specific system operations. And moral explainability may strength the critical mass of public trust through transparent reasoning from metaphysics to morality (demonstrating the ultimate end of the common good and the just means for aiming toward it, with such ethics conducted in the context of the pragmatic demands of competitive cooperation in multidimensional world orders which often deemphasize ethical considerations of population equity and human security). Good AI ethics in healthcare is inherently necessary (as healthcare systems have the duty to do it well and consistently). But it also helps optimize the likelihood of the political stability and economic prosperity of societies reliant on healthy and productive populations and thus for successful healthcare systems integrated with successful PubHealth networks. For healthcare to work now and in the future, it appears it will increasingly require AI technically, and ethics practically to not only show why equity should be a primary strategic objective for systems but also inform how it should be justly and justifiably be achieved. To be equitable, healthcare may require recovering what it means to be personal, but also rediscovering the reality of the human person for whom systems essentially exist to serve. The WHO's 2021 AI healthcare ethics principles may argue that such liberalism-inspired human rights-based principles are critical for the global societal benefit of AIenabled healthcare to become reality, but understanding their metaphysical foundation and pluralistic framework (as proposed by the PSC) may be key to apply and advance them for healthcare system care that patients deserve.

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The future's (AI) thinking healthcare system: blueprint, roadmap, and DNA

9.1 Patients: persons, digits, or both

We commonly agree on the diagnosis that healthcare systems fail, but we disagree to what degree they do (and what their treatment should be). We have spent this book analyzing the multidecade, multinational, and multisector critique, which has argued that systems do not consistently provide safe, personal, affordable, effective, and fair care for populations. If we want different results, we may need a different approach to the years and trillions of dollars spent trying to reform healthcare globally. Instead of retrofitting an underperforming (or even failed) model, we may need to redesign it. Instead of continuing the slowing healthcare system model of the past, we may need a thinking healthcare system for the future. Toward this goal, this book has considered past, present, and emerging designs and trends for healthcare systems in their various dimensions (from precision medicine or PrMed to public health or PubHealth to telemedicine) and societal contexts (from the technical, political economic, and ethical domains). How to fix healthcare increasingly appears to come down not to the lack of sophisticated tools, but of a common understanding of how to design and deploy them.

We therefore have sought to recover and refine an even older and more global vision of self-evident truths stretching across peoples, eras, and belief systems of what the physician-philosopher and scientist, Aristotle, described over 2 millennia ago that appears just as relevant now: reality is the great check on humanity. It is a commonsense, self-evident, and broadly consensus-based first principle that we are rational social animals, unique with embodied vulnerabilities requiring the care of others to come into and grow up, flourish, and give back to this community. As children before we come know the technology, politics, or economics that dominate much of our daily lives, we first know the basic morality of humanity—care for the community that cares for you. We learn early that we are each our own person with unique dignity and resultant rights (with the correlative duties to respect those rights and the reality that the exercise of those rights are constrained by the common good of

the community, which safeguards and manifests our individual good that is fulfilled in it). Thus, the natural tension between human equality and liberty plays out in the tension between healthcare system efficiency and equity. Rather than one side dominating the other, we have explored the concrete cases in which fair and ethical AI is accelerating the translation of this natural tension into a creative tension that produces effective complementariness, achieved by grounding such relationships in the truth of our human reality, like the complementary base pairs of DNA held together and shaped by the double helix of such self-evident truth. The tensions above and between I versus you, individuality versus commonality, localism versus globalism, objectivity and subjectivity, PrMed and PubHealth, artificial intelligence versus human compassion, morality versus power, and so on may thus need to be similarly framed, balanced, and become fruitful. We have explored the theoretical and practical ways and reasons our diverse nations and political economic, healthcare, and belief systems can converge substantively on this moral DNA of the global human family, and together, nourish how it can translate into life for healthcare systems that can survive in our digitalized and divided world, unite the various stakeholders in the globalizing digital healthcare systems, and sustain populations through efficient and equitable operations anchored in the common good. But what does this practically look like? And can we sketch a blueprint and even emerging examples of what the thinking healthcare system model may (likely and should) look like? And can this blueprint enable us to concretely sketch a rough but real roadmap guiding our steps in such a direction, one that can move us from simply seeing digits to one in which we can ultimately see (strengthened through the digital vision) the full person that systems are meant to serve (and even eventually do it well)?

9.2 Emerging blueprints for the future's health ecosystem: form + function

9.2.1 Structural pillars: data, well-being, and integration

This chapter is about bringing it all together—the theories, concepts, and use cases—to consider the emerging blueprints for the future of healthcare systems in increasingly actionable and comprehensive detail (to inform the diverse interests and work of you, the diverse audience, contributing to its birth and evolution). The form of the future's healthcare system as the AI-enabled health ecosystem may be proposed by Deloitte and McKinsey below, and its function may be described by this book's proposed resilient end-to-end integration, operationalized with AI-driven Computational Ethics (AiCE). The preceding chapters have proposed the foundational conception of this integration that recognizes the reality of the inherent and indefinite interconnectedness of the local and global components of healthcare systems, anchored in and stemming from the reality of the human person who is the primary subject and object of

systems' strategic existence. They exist to care for the person. Understanding the modern person in our changing world thus allows systems to survive in this historical moment, particularly by trustworthy and ethical AI-accelerated optimization of efficiency and equity. Drawing on the diverse and pluralistic disciplines, states, healthcare systems, and belief systems, we have considered the proposal on how the reality of the person may provide the metaphysical foundation or moral DNA backbone for the health ecosystem structure of complementary base pairs encoding and giving life to the community: current healthcare systems and future AI-powered health ecosystems, PrMed and global PubHealth, telehealth and patient safety, political economics and ethics, and AI-enabled efficiency and human-centered equity. This system DNA can inform how these pairs fit together with their complementary strengths, held in balance in this DNA of the future's health ecosystem and so enabling an adaptive end-to-end resilience, while avoiding the extremes that otherwise could destabilize the ecosystem.

This book has analyzed the methodologies and results of an evidencebased, multidisciplinary and multicultural, academic, and practical approach to predicting and mapping at least the major contours and content of the form and function of the future's healthcare system model (the book described in its final detail by the fall of 2021 prior to moving through the publication process for a spring 2023 release). Since then while in press, there has been increasing convergence across healthcare and supporting sectors about what this model will likely look like. High-level proposals were articulated in the 2022 reports by Deloitte and McKinsey as leading thought leaders for the pivotal players in modern healthcare (who also help shape its future development), as they respectively rank as the largest and most influential professional consulting services globally (Zimmerman, 2022; Fillion, 2022). Deloitte argued that the world in 2022 is on the "brink of large-scale disruption" as healthcare transitions on our digitalized and divided planet from the present healthcare system model (dominated by attempts at integration of AI-driven technology, complementary stakeholders, and value-based healthcare) to the future model of the health ecosystem (shaped by AI-driven "radically interoperable data, open yet secure platforms, and consumer-driven care") (Dhar et al., 2022). The AI-enabled Fourth Industrial Revolution is projected to continue its rapid transformation of the global political economic order by moving us from "healthcare" and the systems delivering it to "well-being" and the ecosystems nourishing it (with the ambient efficiency and equity defining the expansive definition of health). The three major structural pillars of this health ecosystem model (also categorizing the three major types of "archetypes" of stakeholders) include (a) data, (b) well-being, and (c) integration:

(a) Data: The "foundational infrastructure" or "backbone" of the health ecosystem will likely be dominated by the data architecture that will progressively unite tomorrow's digital infrastructure with today's

organizational infrastructure of healthcare systems, along with the rest of the digital ecosystem underlying our global human society. The archetype contributors to this data dimension of the health ecosystem include data conveners, analysts, and builders.

- i. Conveners specialize in integrating diverse data sources for individuals, patients, organizations, and environments in a shared data architecture, while ensuring its interoperability, security, and privacy.
- ii. Analysts focus on creating, deploying, and optimizing the AI algorithms to translate the above data into insights to accelerate increasingly effective decisions by leaders and clinicians in the health ecosystem (based on optimizing, the likelihood of such decisions will iteratively lead to more desired outcomes, like improved patient outcomes and profitability).
- iii. Builders will design, launch, and improve the components of the data infrastructure (including the interconnected platforms), while helping codify related standards and functionality of the data architecture aligned with the health ecosystem's strategic vision, values, and objectives of the included stakeholders.
- (b) Well-being: The primary legacy stakeholders of the current healthcare systems, including hospitals and clinics (with their related providers encompassing executives, managers, physicians, nurses, allied health professionals, and supportive staff), account for this category. Their strategic present focus on value-based healthcare is expected to increasingly broaden to the broadening and deepening range of consumer-centric digital, virtual, and in-person products and services that prioritize prevention and prediction (without sacrificing acute and rehabilitation care). Healthcare expansion should continue to transition from primarily addressing the individual and negative dimension or deficits in health (including disability and disease) to one that additionally focuses on its communal and positive dimension or enhancement of health (including socioeconomic, psychological, spiritual, and security). Consumer demand in the other economic sectors will likely inform and influence more of the demand for related health products and services as the health ecosystem expands out of local hospitals and clinics and embeds more in the global digital ecosystem and community-based life. The archetype contributors include developers, coordinators, specialists, and hubs.
 - i. Developers will create the wellness software, apps, drugs, devices, products, and programs.
 - ii. Coordinators like today's primary care providers will increasingly coordinate, curate, and assist people's experiences and interactions with the various components, phases, and stakeholders in the health ecosystem. Particular focus areas include virtual, personalized, behavior, and education as wellness care optimizing the continuum of

- disease prevention, chronic disease management, acute care, and rehabilitation.
- iii. Specialists, similar to the present clinicians specialized in particular organs or treatments (especially procedural and surgical), will operate in tandem with coordinators primarily in acute and rehabilitation care when in-home wellness care is insufficient.
- iv. Hubs will locally and physically orchestrate wellness services and products for people in the community setting, including in work and retail settings as adjunct and extensions of people's home-based wellness.
- (c) Integration: The coordinators who cultivate the connections between the data and well-being care dimensions of the health ecosystem will include the archetype categories of logistics, financiers, and regulators.
 - i. Logistics facilitate the just-in-time supply chains delivering wellness products including devices and medications from source to suppliers, spanning likely multidimensional world orders, value blocks, and globalized supply chain stakeholders.
 - ii. Financiers will build on today's healthcare insurers or payors to build more personalized, affordable, and effective finance options (focusing on modular and catastrophic care packages, consumer incentives. advanced risk models, and free market innovation in cost control and value optimization) likely spanning government and private sector
 - iii. Regulators will include those within and connecting government, medical, and technical associations who define, enforce, and adapt standards for data and well-being operations (with a negative dimension that mandates acceptable ranges of operations, services, and products in addition to a positive dimension that incentivizes policy and innovation mechanisms to spur iterative improvement in health ecosystem outcomes for individuals and populations).

9.2.2 Structural features: AI, ambient, and collaborative

McKinsey's 2022 report from its 14th annual healthcare conference of industry leaders and though leaders spelled out the features that flow from the above structure of the future healthcare system model of the health ecosystem (Singhal et al., 2022):

- (a) Data: The two primary features include the following:
 - i. Driven by data andtechnology: AI-accelerated digitalization of healthcare systems is expected to reduce national healthcare expenditures by upward of \$0.56 trillion by 2028 through enhanced productivity, despite declining healthcare workforce amid declining

- demographics principally in the global North (Sahni et al., 2019). These productivity gains are projected to make healthcare delivery more efficient and effective by pairing virtual care with in-home and in-facility care, while integrating standardized data collection and real-time analytics from the above care continuum to guide clinicians' patient care.
- ii. Transparent and interoperable: Government and professional association-driven regulatory innovations are accelerating more accessible and reliable data interoperability with price transparency. The new mandates from the US HHS ONC's Cures Act Final Rule (introduced in the above ethics chapter) are being implemented by the fourth quarter of 2022 to better streamline patients and providers' free electronic health record (EHR) access, accelerated by ONC requirements for EHR vendors and healthcare industry actors to utilize secure, standardized, and publicly available APIs while avoiding information blocking (allowing payers, providers, and technology firms utilizing even unstructured EHR data to develop better care delivery tools through enhanced interoperable data collection) (ONC, 2022). Additionally, a US HHS federal rule went into effect in July 2022 requiring health insurers to publish the negotiated prices they pay providers for healthcare services, following a January 2020 rule requiring hospitals to publish their negotiated prices (though with slow compliance up to the fourth quarter of 2022, there are growing signs of increasing price transparency to enable patients to shop for different healthcare services based on a more informed approach to comparing competitors who must in turn compete by quality and/or cost for consumers) (Kona and Corlette, 2022).
- (b) Well-being: McKinsey highlighted the following three features:
 - i. Enabled by new medical technologies: New innovations are delivering better clinical outcomes, closer to home, and at cheaper costs, including with remote monitoring (i.e., for patients with dementia, atrial fibrillation, or those pregnant), automation (i.e., open-source and sensor-augmented insulin pumps linked to smart phones to improve time in target glucose range by adjusting insulin delivery better than patients adjusting insulin themselves), and communitybased care (including digital health-enabled community-centered care such as with the MOMS California-based program cost efficiently improving birth outcomes with AI-enabled personalization of human-in-the-loop intrapartum care and wearable IoT tracking physical and psychosocial data) (Burnside et al., 2022; Rodrigues et al., 2022).
 - ii. Patient-centric: Among providers featuring patient-centric digitally enabled care, over 60% of their patients by 2021 expect the digital ability to check EHR test results, renew medications, and schedule

provider appointments, while they are nearly six times more likely to utilize other services from the same provider, 28% less likely to switch providers, and have 36% fewer unnecessary provider visits allowing increased profitability for such providers compared to providers lacking such digitally enabled patient-centric care (Singhal et al., 2022).

- iii. Virtual, ambulatory, and in-home: These features are manifested emblematically by the US telehealth company, Amwell, which launched in 2021 its Converge platform with an open data architecture, enabling diverse digital health applications from diverse partnering vendors to be housed under the same digital roof with a single code base, including leveraging the complementary comparative advantages of Google Cloud (with its NLP and other AI-based data storage and analytics including for real-time clinical insights, patient translation, and provider captioning), TytoCare's handheld exam kit (allowing remote providers to examine patients), Cleveland Clinic (for second virtual opinions from over 550 medical subspecialist clinicians), and BioBet (for continuous remote vital monitoring with AI-enabled early warning score system for providers) (Landi, 2021).
- (c) Integration: Three key features are highlighted by McKinsey suggesting how the twin data and well-being dimensions of the health ecosystem are expected to operate with successful interdependence.
 - i. Integrated yet fragmented: As the majority of the world's national healthcare systems are expected to increasingly digitalize and leverage technology company's external capacities synced within their systems, even the United States as arguably the most fragmented national healthcare system is expected to witness even more of the already notable "integrated yet fragmented" movement toward unifying value-based healthcare (Singhal et al., 2022). Innovative companies and public-private partnerships are projected to continue competition within distinct phases of well-being and the clinical care continuum by drawing on AI-enabled data interoperability, digitally and practically connecting the stakeholders of the health ecosystem for the lifecycle of each patient interacting with the ecosystem. Such approaches on the integration spectrum, from "one-stop shop" (i.e., Amwell above) to vertical and horizontal integration (i.e., Big Tech in the political economic chapter partnering with payors, providers, and patients) to truly nationalized systems like the NHS, are expected to simplify the complexity of the health ecosystem for patients to increasingly have on-demand healthcare and wellness in a more accessible, affordable, and fair manner. It is theoretically possible for an AI-enabled truly integrated and comprehensive health ecosystem, such as with the British National Health Service (NHS) or Chinese system providing not just a comprehensive but also a complete

ecosystem where all aspects of digitally enabled wellness are available, accessible, affordable, and equitable for all patients—though such a complete model appears so far in the future that it is difficult practically to offer meaningful details on the model or the steps to actualize it (given the widespread failures of Big Tech and the largest government and private funders in the world who have thus far failed at this breadth and depth of integration, atomized or fragmented integration seems the most likely approach for the foreseeable future, which will likely in turn significantly influence this potential deep future or next phase of complete health ecosystems following the future's next evolutionary step of health ecosystems this chapter discusses).

- ii. Value-based and risk bearing: Funding transformation increasingly and globally on both ends of the spectrum of healthcare system models (from the more privatized end of the United States to the more public delivery and funding models of the British or Chinese) is prioritizing risk sharing value-based financing as growth is projected for management services (doubling) and ACOs (up to 22% of insured patients in the United States alone) (Singhal et al., 2022). By focusing on well-being and the nearly 90% of health outcomes attributed to lifestyle factors including nutrition, fitness, and socially contextualized risk factors, such financing models seek to incentivize providers to keep more of the profit by delivering better outcomes.
- **iii.** Funded by private investors: Venture capital and private equity deals in healthcare grew at a 1350% faster annualized rate than nonhealthcare deals from 2014 to 2021, as AI-driven digitalization has growing financial wins showing short in addition to long-term ROI through value-based healthcare that is more effective, affordable, and equitable (Singhal et al., 2022). As the telehealth chapter introduced, these deals notably are increasingly multinational as such players expand from the more saturated markets in the United States and Europe to the more emerging healthcare markets in South America, Middle East, Africa, and Asia (especially as AI players are progressively global in scale to leverage a growing network of multinational actors who not only allow greater market growth but also collectively account for integrated healthcare delivery services).

McKinsey's 2022 report thus highlights how an AI-driven, ambient approach to wellness in the health ecosystem that leverages collaborative partnerships from diverse stakeholders is expected to increasingly fill out this model of the future healthcare system that Deloitte structurally summarizes. NEJM echoes the Deloitte and McKinsey vision (Zimlichman et al., 2021), yet the means of attaining it (and doing so fairly across the global human community) are still ambiguous.

9.3 Fleshing out the details: the future's Al-enabled health ecosystem

Such leading global voices are key, yet they leave unanswered (a) practically how do we to get that vision and (b) fundamentally how do we do it in our globalized world (that exists not just in the US, Chinese, and European markets where most of the current healthcare AI innovations are occurring, principally for the near-term benefit of high-income populations). We will therefore highlight the practical and unifying elements from the preceding chapters of this book to attempt to answer the above questions. The above thought leaders may give us a helpful but still incomplete sketch of the future of healthcare systems in terms of its structure or form, so we will consider now how to flesh it out through how it can function for AI-driven efficiency and equity (through the unifying framework of AiCE-driven resilient end-to-end integration).

9.3.1 Resilient integration in the health ecosystem DNA: data + well-being = efficiency + equity

Structurally, the above future's health ecosystem model emphasizes how health is local, but the ecosystem is global. Functionally, resilient integration emphasizes how the data and well-being dimensions of this ecosystem can be complementarily united in the "health ecosystem DNA," like in the moral DNA of systems introduced in the AI ethics chapter. We have considered throughout the book how AI-accelerated healthcare Big Data (or AI-HealthBD) drives efficiency, and this efficiency at scale equals equity (effectively delivering value-based care fairly across populations). And as the above sections introduced, McKinsey and Deloitte's 2022 reports converge and are superseded in breadth and depth with this book's cumulative proposal on how data in a holistic ecosystem approach can drive well-being not just healthcare, and thus at scale begin to approximate global well-being. For as the political economics chapter introduced with the J-curve and the various societal models ranging from autocratic socialism to democratic capitalism (with state-centralized capitalism in between the above poles, though closer to the former), political stability can be undermined not simply by societal economic stagnation but also by individual health stagnation. It is thus in the personal interests of individual leaders and collective masses to avoid excessive inequality. In the health dimension of societies, wealth and health are complementary, as are poverty and sickness, and thus stability and security (with human security through effective healthcare producing collective state security at scale). If a nation's healthcare system fails to address sickness and human insecurity at this sufficient scale, poverty and inequalities can metastasize and jeopardize the sustainability of the society and its national security. We thus can approach the health ecosystem DNA built on the ultimate convertibility of

data and well-being, efficiency and equity, and value and value-driven AI integrating the initial complementary ends on both sides of this equation. As we have explored throughout this book, AI-driven value-based healthcare operates in a health ecosystem's political economic framework, emanating from the communal moral foundation it manifests with its underlying values and common beliefs that hold societies together (both locally and globally). Resilient integration unites the required organizational (of the health ecosystem actors including providers and payors), technical (of the AI-HealthBD embedded in the data architecture), and moral (of the common values in the global health ecosystem, which the ethics chapter proposed through the prevalent global moral framework of dignity and rights, articulated by the Universal Declaration of Human Rights [UDHR] and the Personalist Social Contract [PSC]). This resilient integration can allow substantive innovation and progress on this value and value-driven AI comprehensive structural integration of data and well-being, practically expressed in efficiency and equity at scale. The function of the future's health ecosystem can thus be expressed essentially in its ecosystem DNA guiding and managing the relationship of complementary poles: data and well-being, health and wealth, localism and globalism, individual and community, political economics and ethics, PreMed and PubHealth, telehealth and patient safety, openness and stability, liberty and equality, dignity and security, and efficiency and equity.

9.3.2 Practical key to the future's AI health ecosystem: complementary ecosystem pairs

To get to the final practical part of this chapter about concrete exemplars of the emerging model of the future's health ecosystem, let us bring together the above theory with how this book has tried to flesh out the form or structure of the model by understanding how it functions. How does the ecosystem come to life from its above DNA, rooted in the reality of the patient as a person? Let us therefore analyze how the below complementary pairs (introduced in the above complementary chapters) through resilient integration can put flesh on these conceptual bones to deliver efficiency and equity in present healthcare systems' transition to the future's AI-enabled global health ecosystem (Fig. 9.1).

The healthcare system and AI overview chapters highlighted the relationship between the diagnosis and treatment of modern healthcare. Consistent with the high-level projections from the world's thought leaders (articulated by Deloitte, McKinsey, and NEJM above), these chapters sought to detail the concrete specifics of why healthcare is underperforming (because of its poor quality, safety, prevention, and cost) and how it may be remedied (by AI accelerating its digitalized, personalized, globalized, and equitable transformation), with a cumulative result of value-based healthcare consistently for patients and populations. The AI chapter particularly highlighted this process

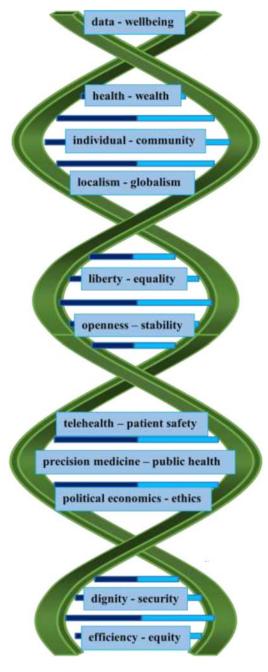


FIGURE 9.1 The future's health ecosystem DNA.

from the standpoint of the digital integration of current healthcare systems with the global digital ecosystem (with the projected end product of the global health ecosystem within and in parallel with the overarching digital ecosystem). The chapter discussed how this transformation is progressively gripping healthcare, driven by the AI-based Fourth Industrial Revolution. The data architecture for the health ecosystem is expected to increasingly rely on iterative quality improvement and embedded, trustworthy, collaborative design to enable a transparent, effective, and equitable governance with broad patient and societal support (for the health ecosystem that progressively delivers more and more on patient/consumer needs).

The PrMed and PubHealth chapters highlighted the necessary pairing of parallel and interdependent patient and population care, to ultimately optimize the health of both concurrently. The PrMed chapter described how the PrMed emphasis on AI-driven data science is increasingly facilitating the clinical translation of multiomics (complementing larger medical care) into effective personalized care. When scaled, it approaches the level of population health (or PopHealth) within healthcare systems and the level of PubHealth within societies (nationally and even globally). The PubHealth chapter in turn highlighted the historic transition from a Western dominated global agenda and funding priorities to a postcolonial global PubHealth. This frames also the current transition from data imperialism and colonialism to a more inclusive, multicultural, and local-driven PubHealth governance in which the dominant AI power players (typically US, Chinese, and European governments and corporations) develop health data architecture and functionalities in partnership with Global South PubHealth systems and national leaders who set their own strategies and operating parameters (rather than simply being data sources for external AI firms leveraging them for the sole or primary benefit of the Global North). This local globalism approach—prioritizing sovereignty, solidarity, and survival—helps map emerging concrete partnerships in which AI is accelerating PubHealth efforts in traditional domains (i.e., as vaccines, nutrition, and poverty-related chronic and infectious diseases) and leading-edge domains (integrating such efforts with PrMed to complement acute and chronic care in legacy healthcare settings including hospitals).

The telehealth and patient safety chapters attempted a more granular assessment within the above AI-driven PubHealth—PrMed partnership. AI-driven telehealth advances are powering extension of current healthcare systems to more patients and populations (including low-income and traditionally excluded groups), while patient safety is focusing on improving the quality delivery of care within such expanding boundaries. The telehealth chapter discussed how cloud, fog, and edge data architectures and computing are enhancing the digital integration of legacy healthcare system with the inclusion of emerging partners in the health ecosystem including remote care actors, payors, private corporation, government, and PubHealth systems and programs. As healthcare systems expand digitally, this enhanced data flow and

functionality enables more rapid, effective, and equitable care especially in resource-limited areas including rural, inner city, and low- and middle-income nations including those with healthcare worker shortages (while also increasing system complexity and risk, and thus the need for enhanced safety countermeasures). The telehealth chapter additionally focused on the usage and surge of global internet and telecommunications that are exponentially growing the global digital ecosystem, with dependent data security and safety measures, while innovations such as nonterrestrial and AI-augmented governance of digital, electrical, and internet connectivity networks are lowering the digital divide for more populations to benefit from telehealth. The patient safety chapter in turn built on data security and safety initiatives with telehealth to institutionalize and digitalize effective safety measures, establishing a minimum "floor" for acceptable healthcare delivery. Such measures were built on WHO standards (and their derivative and informed national, professional, and health system standards) while testing new AI-driven safety products including drug safety, clinical reports, and alarms to prevent, mitigate, and respond quickly to healthcare system errors and patients' dynamic diseases. The broad emerging trends in such AI-driven safety measures, both internally to healthcare systems in their legacy hospital-based care and externally through their telehealth extensions in patients' communities, focus on embedded, ambient, command center, and blockchain innovations to ultimately optimize transparency (antibias), reproducibility, explainability, and effectiveness of such AI advances.

The final two complementary chapters or AI-driven health ecosystem base pairs included political economics and ethics. The former chapter focused on the evolutionary biology and historical trajectory framing the societal context in which healthcare systems are operating and evolving, including genetic evidence (for our seeming innate and ubiquitous proclivity for collaborative competition) and global development (from early Western modern industrialization precipitating the ideological conflicts of WWI and WWII, unleashing an American liberal capitalist and democratic domination, digitalization, and globalization up to the 2010s). By the COVID-19 pandemic birth in 2020, we analyzed how the new multidimensional world orders (digital, security, economics, and ideology) were increasingly defining the potential and limitations of the healthcare sector globally. With the democratic capitalist US and more autocratic state capitalist (and increasingly socialist) China locked from the 2020 onward in a progressively overt great power rivalry (principally dividing the world with their arms race for the future's dominant high-end AI-driven digital technologies, including chips, semiconductors, quantum computing, and their weaponization in a global security and military buildup), the rest of the Global North and South are segmenting more into alliances and value blocks (as the US and China deploy sanctions, tariffs, and export controls against each other, concurrent with US allegations of China's theft of US intellectural property). Concurrently, the majority of the world up to at least the end of 2022 (as of the writing of this book) are increasingly uniting in at least quiet support of national sovereignty and security, including the defense of Ukraine against Russia's alleged genocidal invasion of it. The increasingly autocratic Russia (with Iranian and North Korean weapons' support [even amid China progressively distancing itself from Russia practically though remaining supportive to some degree rhetorically]) is sharpening the ideological divides between the more democratic and more autocratic value blocks globally.

Such political economic headwinds are challenging the AI digitalization of healthcare systems, which increasingly require global supply chains, public-private partnerships, and professional associations that can be endangered by such conflict and competition, grinding at the edges of the tectonic plates of shifting power blocks in the multidimensional world orders. The chapter further considered how health systems can get caught amid this rivalry, with the dueling critiques from autocratic power blocks that democratic ones are divided and inefficient, while democratic blocks counter that increasingly autocratic regimes like in Russia, Iran, and China sacrifice longterm citizens' rights, government accountability, resilient sustainability (through internal corrective mechanism on inevitable despotic rule), national security (engaging in violent internal and often foreign conflicts to maintain domestic control), and economic growth (by imposing the will of the few on the innovative entrepreneurship of the many, despite the practical impossibility of a few managing the complexity of the market of the many), leaving autocratic central planning to champion equality at the expense of liberty and thus losing both, while democracies champion equality in freedom to preserve both (Kotkin, 2022; Hayek, 1944). We thus analyzed in the peer review medical literature how social welfare democracies leverage the prosperity of the markets in this political economic framework to produce what empirically appears to be the most effective, efficient, and equitable individual and PopHealth (with free and open societies generally being progressively healthier and wealthier than more controlled and closed societies), while acknowledging that the more autocratic state capitalism model, that is, of China does have the potential to make its own notable and novel gains.

We thus concluded the political economics chapter on its concrete relevance for the future's emerging health ecosystem model. We explored how PubHealth + human security = political economics + national security, particularly as current healthcare systems transition to their AI-enabled health ecosystem version, with progressive frictionless and seamless integration with society (nationally and globally). To optimize the efficiency and equity of such AI-driven healthcare of the emergent future, the potentially necessary measures the chapter explored to realize this vision include the following. The global investment in "moral political economics" appears to help correct deficiencies in societal structures (i.e., discrimination and underinvestment of healthcare resources for low-income or minority populations) by reanchoring

political economic structures in our common moral beliefs or first principles about the dignity of every person to counterbalance destabilizing effects of excessive societal power consolidation that ignores this reality. "Guard rails" of diplomacy (i.e., through PubHealth and clean energy) and deterrence (in digital qualitative edge of security alliances) in global governance are promoted to strategically manage inevitable conflict, and thus minimize the risk of competitive collaboration (collaboration on existential threats like disruptive AI technologies and climate change, in parallel with competition in digitalized security) from spilling over into catastrophic conflict (and even World War). Healthcare is emerging potentially as the key strategic guard rails, particularly with AI-enabled global PubHealth advances in pandemic management, climate change countermeasures, poverty (including hunger and dirty water), and communicable and noncommunicable diseases including with the WHO and private-public partnerships in the East-West and North-South). Additionally, the push from "digital colonization" to "open healthcare" focuses on more equitable mutual benefits of digitalization for low-income communities, healthcare systems, and nations.

The ethics chapter built on the political economic chapter to explore the more foundational societal challenges and possible solutions for efficient and equitable management of societal resources, particularly in healthcare. The chapter analyzed the birth of global standards for AI ethics especially for health, beginning with the 2020 Rome Call with the UN, Big Tech, and multicultural and interreligious collaborations to explicitly ground such highlevel consensus on modern ethics and international law, including explicit reference to such modern ethics and international law anchored in the UDHR's "recognition of the inherent dignity and of the equal and inalienable rights of all members of the human family" which serves as "the foundation of freedom, justice and peace in the world" (UN, 2022; Monlezun, 2022; Monlezun, 2020). Aside from a more simplistic historical account of humanity's ideological trajectory for mutual survival, modern existential crises following WWII emphasized the need for a basic moral recovery of our common humanity and the derivative self-evident realizations of our intrinsic dignity or worth entailing individual and communal rights, with their correlative duties to honor such rights that collectively account for the common good (achieved from the empowered pursuit of each individual exercising her/his rights to advance the common good and so realizing her/his own good in the process). We further explored how the PSC may help articulate and defend such insights through the collective strength of the world's converging consensus of our diverse belief systems (both religiously unaffiliated and affiliated), serving as a substantive methodology to ground and guide healthcare reform efforts and its transition to the future's AI-enabled health ecosystem. As AI is a tool, we need common moral beliefs to guide our strategic development and deployment of it in healthcare to achieve a mutually desired future in which equity, rights, and diversity are not sacrificed for efficiency, control, or power consolidation. This PSC perspective may help support the substantive justification for this to a detail and degree that facilitates the shared solutions to practical problems emerging in healthcare reform, redesign, and AI-driven transformation. We explored through this lens therefore the recent transition from the 2020 Rome Statement to the 2021 WHO global standard attempt for AI ethics in healthcare to more recent theoretical and concrete innovations. These included the translation of data interoperability to moral interoperability to facilitate the convergence not only of diverse stakeholders, strategies, and data sources and capacities in the health ecosystem but also of their diverse underlying belief systems which inform them (with dignity being the common denominator or common moral language and architecture to resolve disagreements and align interests and capacities to the common end of humanity's common good, including for health ecosystems orientated to the health dimension of that good). The ultimate practical insight of the above is that if the health ecosystem is to optimize health, it must understand what health is and thus fundamentally who is the person who is either sick or healthy, and thus how to use AI as a means to the end of this well-being (individually and societally). Pluralism becomes a necessary means to the clearest vision of this, not a hindrance to or counterargument against a real and shared vision of it being necessary or even possible. Understanding the reality of the person and humanity thus empowers the health ecosystem to wisely use AI well to accomplish its central duty of preserving and nourishing life (avoiding ideological imposition or political economic power grabs). Building on this conceptual foundation, we then analyzed concrete innovations in health AI ethics including embedded ethics in general and AiCE (policy analysis) in particular, including how AiCE has been deployed to integrate AI ethics for real-time clinical support in a continuous iterative cycle improving the design, deployment, and optimization of AI-enabled clinical efforts such as addressing racial disparities in cardiac arrest while optimizing its outcomes.

9.4 Health ecosystem: practical emerging cases

You made it this far, intrepid reader. In these final two sections of the book, we will now analyze the practical emerging use cases that may illustrate this integrated vision of what the future's health ecosystem may look like, and how those cases are suggesting the development trajectory away from today's healthcare systems. To keep this conceptual and concrete vision as organized and informative as possible, we will structure this section by starting with its global dimension and zooming in progressively to it strategic, structural, local, operational, and functional levels. This tangible vision will then allow us to transition to the final section of this book in which we will finish with a synthesized high-level and distilled down summation of what the future of health essentially is, and how to get there (weighted by the confidence of the predictive data underlying the model).

9.4.1 Global, strategic, and structural: Al-powered health

This book has essentially proposed that today's siloed, localized, hospitalbased healthcare is rapidly becoming tomorrow's AI-driven globalized, digitalized, ecosystem-embedded well-being. This fundamental (perhaps even inevitable and irrevocable) transformation is being powered by the early 21st century's Fourth Industrial Revolution's AI-accelerated digitalization that connects traditional healthcare systems not only internally to their constitutive components (patients, payors, and providers) but also increasingly externally to their emerging partners (communities, corporations, academics, governments, and international organizations), which stretch across international supply chains, nations, healthcare systems, cultures, and belief systems. AI is challenging the foundation and redefining essential aspects of healthcare, imbuing it with the capacity to be a smart system (improving itself while improving its fundamental function and structure to ultimately improve its value-based patient outcomes). Therefore, this book has by necessity attempted a foundational and integrated rethink of how healthcare can become a thinking healthcare system, aware of itself, its strategic purpose (maximizing efficiency concurrent with equity), and ethically bounded operating parameters (grounded in the reality of each patient as a person, safeguarded by the common good in a pluralistic world). This system awareness and design thinking derives from the collective awareness of the growing list and diverse backgrounds of the thinking systems' stakeholders. But practically, what does this look like (and increasingly what will it)? And importantly in its pursuit, how does the future's thinking healthcare system avoid "strategic sedation" (of just staying alive as a healthcare sector, a passive victim to the concurrent societal, technological, and economic forces)? How does the future's healthcare system rather become a dynamic and deliberate actor shaping its needed future, by progressing toward the measurable and meaningful shared vision of its mission (delivering value-based healthcare, defined as such by its efficiency and equity, maximizing individual and population well-being)?

An emerging case of global and strategic elements of the future's AIpowered health may be Mayo Clinic's global network. Organizationally, Mayo leverages its growing global network of partners, joint ventures, and facilities to sustainably maintain their top position in value-based healthcare for over 3 decades, expanding care to rural and underserved communities, attracting \$1 billion in research funding, and generating \$15.6 billion in revenue annually (Definitive Healthcare, 2022; Mayo, 2018, 2021). According to the US ACA Hospital Value-Based Purchasing Program (linking Medicare payment to the quality of care, calculated as the equally weighted product of clinical outcomes, safety, person and community engagement, and cost efficiency), Mayo's three US major medical campuses are nearly double the provider reimbursement than the second best hospital in the country. This value-based healthcare is delivered at scale as Mayo remains one of the largest

physician groups (at over 12,000 physicians), utilizing its Mayo Clinic Health System which spans over 15 hospitals and 52 multispecialty clinics across three states (targeting rural and underserved communities) and global referral and partner network (Mayo, 2022a, 2022b). This global network features clinics (in the UK through an initial NHS partnership), referral offices (in China [partnered with its national healthcare system], India, Canada, Colombia, Dominican Republic, Ecuador, El Salvador, Guatemala, Honduras, Mexico, Panama, and Peru), joint ventures (with the United Arab Emirates's Sheikh Shakhbout Medical City and China's Valurise Health Solutions and WuXi Diagnostics), and Mayo Clinic Care Network (of 40 member hospitals in the United States, China, the United Arab Emirates, South Korea, Singapore, Saudi Arabia, and Mexico to augment local healthcare with Mayo's global clinical expertise and referrals to their main campuses as needed).

The digitalization and commercialization of Mayo's value-based healthcare expertise leverages this global network of partners and centers to enhance the local care of communities (including its medical knowledge capital and diagnostics, including through its Mayo Clinic Laboratories). This network is accelerated by the Mayo Clinic Platform with an AI-HealthBD approach to integrate ecosystem partners through strategic alignment to the common end or mission: "inspiring hope and promoting health through integrated clinical practice, education and research," driven by its "primary value" that "the needs of the patient come first," as "an expression of the vision and intent of our founders, the original Mayo physicians and the Sisters of Saint Francis," reflecting the common moral vision of personal dignity orientated to the common good (Mayo, 2022c). The clinical mission of the Mayo Clinic Network is enhanced by Mayo's Platform twin signature program, Mayo Clinic Platform_Accelerate, focused on catapulting early-stage health tech AI start-ups to market readiness through venture capital, deidentified data, validation frameworks, clinical workflow planning, and technical and organizational mentorship. The AI-accelerated strategic expansion globally (through partner, expertise, referral, and technology networks) to better deliver healthcare locally is generating a progressively dynamic and deep international data architecture, enabling and empowering an increasingly AIaccelerated well-being approach to the future of health. This structural framework (of collaborative integration of AI-driven data and ambient wellbeing for the future of healthcare) is grounded, sustained, and guided by its moral foundation. This moral interoperability derives from and is articulated by the vision of the first Mayo father and brother physicians (responding to the plea of the Catholic sisters asking them to care for their tornado-struck town). It was the foundation for St. Mary's Hospital, which the sisters funded and staffed to enable the physicians to begin and end their treatment of each patient as a person, a neighbor, or a friend, and in turn St. Mary's became the historical foundation and standard for its global network since. This local moral vision through nearly two centuries evolved to become a global organizational

vision, realized by its strategy-informed operations, and manifested by its structure of AI-enabled Big Data architecture animating its ecosystem of likeminded partners united in this common dual vision.

9.4.2 Local, operational, and functional: maturing enterprise-wide Al-powered health

There are a number of additional innovations to this potentially competitive model for the future of healthcare that demonstrate case uses of how these global, strategic, and structural elements can be effectively integrated and deployed at the local, operational, and functional levels in a process of AI maturation in the future's health ecosystem. Picking up from the last section, the next steps for Mayo Clinic's AI deepening digitalization and globalization to enable efficient and equitable value-based healthcare locally center on its enterprise-wide digital strategic transformation. Mayo in 2020 named a Chief Digital Officer and created its Center for Digital Health to accelerate the Mayo Clinic Platform (with its Accelerate and Network programs) and similar initiatives through strategic alignment consistent with its vision and values, testing and scaling AI-driven innovations in value-based healthcare, orchestrating system-wide efforts (avoiding inefficient redundancy or perpetuating underperforming initiatives), and guiding the dynamic balancing act between standardization of best practices and personalization for local needs (Davenport and Bean, 2022). Moving from specific and narrow use cases to more general and adaptive use, such enterprise-wide AI strategy entails shortening the pipeline from "multimodal AI models" design to "disciplined experimentation" (rapidly validating, optimizing, and safeguarding model performance in real-time clinical care within carefully defined and monitored multidisciplinary safety parameters) to sustainable and adaptive clinical implementation. Such efforts focus on generalizing the design and approach of current narrow uses like AI augmentation in radiographic image and electrocardiogram data analysis to more general autonomous image analysis, diagnosis, and treatment augmentation (with application for laboratory, pathological, and physical exam testing and the wider acute and chronic disease management to the broader preventive care and well-being optimization).

Moving from local identification of clinical problems to operational and functional AI health use is being sped up by Mayo's "discovery-translationapplication research continuum" in health-tech partnership with Google (Davenport and Bean, 2022). This AI factory approach since 2021 has focused on expanding faster enterprise-wide AI use cases (numbering 200 use cases since launch) that identify, standardize, scale, and adapt best practices in AI software, development, and technology processes, aided by Google's Cloud Platform and Google Health to leverage the private sector's technical expertise synthesized with Mayo's clinical expertise. Enterprisewide health AI strategy informs the use cases that are sought, the AI factory accelerates their testing and optimization, the Center for Digital Health facilitates their system-wide orchestration, and the Mayo Clinic Platform informs the continuous and iterative quality improvement cycle of the above to connect external digital health ecosystem partners (consumers and producers) with its internal stakeholders applying the AI health use cases at scale globally. The system-wide AI strategy additionally allows more effective triage and management, including deprioritizing resources for the more mature radiology and cardiology clinical domains to focus on the less mature other specialty areas, while advancing concurrently the needed transparent and fair governance (grounding the above iterative cycle within consensus-based ethical parameters bridging diverse stakeholders, nations, legal systems, healthcare systems, and belief systems).

The 2022 report from Deloitte's US-India team on enterprise-wide health AI strategy (building on its survey and interview work with 2875 global technology and health executives) has particularly helpful advances for the local level as organizational and technical advances allow progressively better efficiency, equity, and risk management through enhanced cost reduction, patient-consumer engagement, effective communication operationalization of health AI strategy, and identification of optimal ecosystem partners supplementing healthcare system deficiencies and weaknesses (Chebrolu et al., 2022). To operationalize the AI strategy at an effective functional level, tech and health executives are increasingly identifying the remaining challenges of AI-related ethics, cybersecurity, shifting regulations, automation-associated job losses, model failures, limited explainability and transparency, and consumer and employee distrust. In addition to the data interoperability and governance advances, we discussed in the above chapters, enterprise-wide AI strategy is the additional dominant executive response to these challenges that has a growing success track record addressing such challenges.

Successful local translation or maturation of an effective global and structurally sound AI health strategy is being centered according to such executives on their organization's coordinated efforts to cultivate leadership support, technical and professional talent, and ecosystem partnerships (Chebrolu et al., 2022). Enterprise leaders need to understand the necessity of AI's unique role digitally transforming healthcare systems into the future's health ecosystems (consistently, sustainably, and fairly delivering value-based healthcare) in order to define, communicate, and adapt the needed enterprisewide AI strategy to realize that vision. Cultivating talent that is technical (algorithm design and project management) and professional (adapting projects for application with nontechnical partners) is required to implement such strategy successfully at an operational level, as healthcare systems are adjusting their workflows and workforces according to these executives globally to attain the related measurable goals and milestones. Teaching

providers enough of AI (to enable them to communicate their needs and those of their patients) and AI engineers and scientists enough of healthcare delivery (to enable them to communicate possible solutions to providers) is increasingly enabling effective dialogue, codesign, development, and optimization at the local level of such strategy. Effective enterprise-wide AI strategy and local operationalization with growing internal talent additionally require correct selection and alignments of health ecosystem partners when external functionalities and capacities are required, particularly through buy versus build decisions when internal resources are insufficient. Executives universally identified IT, cloud, and professional consulting partners as critical to this AIenabled transformation of their healthcare systems, particularly with the growing options of such partners offering more sophisticated and comprehensive platform-enabled digital health ecosystems. Legacy pipeline businesses specialize in aspects of the linear supply chain (i.e., manufacturing, sales, delivery, etc.) linking producers to consumers. In contrast, emerging platform businesses specialize in data-driven integration of a cyclical supply chain in which enhanced products and services are identified, created, and optimized through a continuous feedback loop of producers and consumers. Such platforms for healthcare systems increasingly provide tailored packages of technical AI-enabled digital products and services (i.e., data architecture, model training and validation, cloud storage, etc.) allowing systems to maintain on their legacy focus on clinical and organizational workflows and outcomes, but in emerging platform-enabled health ecosystems that can more efficiently and accurately allow them to expand to new populations, capabilities, and revenue streams, while cultivating more preferred, integrated, and comprehensive patient experiences of the ecosystem.

According to the growing consensus of tech and health executives, the main process template for mature enterprise-wide AI strategy that is successfully operationalized locally for healthcare systems focuses on AI-enabled digitalization of the current healthcare linear value supply chain: operations (products, pricing, marketing, etc.), consumers (patient enrollment, access, engagement, etc.), clinical (prevention, care delivery, research, etc.), performance (product supply chain, compliance, revenue cycle, etc.), and workforce (administration, clinicians, etc.). Successful AI strategy translated to the dayto-day functional level for the top performing healthcare systems increasingly appears to respectfully focus on transformational capabilities of the above steps: digital authorization (frictionless and rapid decision-making), personalized experience ("omnichannel" or seamless, high-quality system engagement with patient-consumer needs), AI-enabled well-being (integrating and elevating healthcare products and services to the level of consistent value, efficiency, equity, safety, and reliability), autonomous ("always-on" trend and anomaly identification), and smart workforce (optimized talent and resource recruitment, retention, cultivation, and allocation).

9.4.3 Emerging transformation trends: dignity-security, strategic empathy, adaptive empowerment networks, embedded clinical trials, digital twins, quantum health, and liquid AI in cloud EHRs

There are several key emerging trends capturing the projected directions and details of the above transformative elements. There is growing consensus that their strategic and technical advantages compared to their competing alternatives can help facilitate and inform the transition from current healthcare systems to the future's AI-enabled health ecosystem to complement and catalyze the above global, strategic, structural, local, operational, and functional major elements. They focus on integrated force-multiplying solutions to the organizational, technical, and multicultural or moral challenges emerging from the above transformation process in the framework of resilient integration previously discussed:

(a) Global: Human dignity-security

- i. Generally, the Global West's ideological, cultural, and political economic foundational emphasis on dignity and the East and South's emphasis on security may unite in a dignity-security complementary spectrum or relationship interface, converging from different angles on the same integrating point of health AI security (which can strengthen ties across such typical divides including for healthcare systems which must traverse them to deliver care). Whether the West's focus on the individual, dignity, and rights or the Rest's focus on the community, security, and duties, both spheres generally recognize the central importance of safe and reliable AI in healthcare. There are a number of emerging concrete developments that suggest this may be a productive common global language or framework in the transformation of modern healthcare systems.
- ii. The UN's 2003 Commission on Human Security and the related subsequent WHO initiatives have promoted "human security" as the conceptual intersection of individual dignity and national security, safeguarding human persons as the most vital resource and asset of nations and thus individual's dignity, survival, livelihood, and equality, which collectively account for the justice, sustainability, flourishing, and stability of states (Ogata and Sen, 2003; Brown et al., 2022).
- iii. Necessary for human security in the future's emerging health ecosystem is AI security, describing the limiting operational parameters (i.e., safety, reliability, and privacy), which complement its counterpart of AI performance (i.e., the maximizing performance parameters of efficiency, effectiveness, and speed). Following recent scholarship and "health diplomacy" included by the UN Development Program, AI security requires coordinated global collaboration with shared expertise, technical resources, and local governance on such concrete persistent threats, which range from cybersecurity,

authoritative suppression of transparent and true information (especially by autocratic regimes), social media-accelerated demonization, not simply polarization through AI-based algorithms increasing user engagement through preying on fear and anger (especially in democratic regimes), and inequitable disruptive effects of AI technologies (particularly in the developing world) (Roff, 2017; Tapia et al., 2022).

- iv. Fundamental to the emphasis of human dignity and security (supporting the common principle of health AI security from complementary angles) informs the pluralistic consensus that the good healthcare system must know the destination or end of good healthcare (good insofar as it achieves its good mission of facilitating wellbeing for its patients efficiently and equitably), and thus the good means to achieve it (Monlezun, 2022). Such good AI ethics bridges and informs good AI technology, and so bridges diverse health ecosystem, its partners, peoples, and belief systems, while leveraging such diverse perspectives to better see the common unifying vision of what Aristotle described as the good of humanity (which the health ecosystem serves via well-being central to its realization). The UN's post-WWII 1948 UDHR and derivitive instruments onward (including the WHO and its health AI ethical and technical strategies, standards, and solutions) have operated with the dignity and securityguided common principle that regardless of our state or beliefs, we exist in a shared reality in which we find ourselves (and thus we can share certain minimum common values that bind us together). This foundational first principle anchoring us in a common existential identity and home avoids the Western-dominated "philosophical vertigo" accompanying the ideological conflicts of the last century (that also undermine effective health collaboration including on pandemics, poverty, and climate change) by the asserted rather than rationally defended axiom that we are simply radically autonomous agents who construct our own reality, including whatever moral duties we wish to assign or not assign to ourselves, rather than unique persons belonging to a global human family bound by a common humanity, good, and duties to it. This global dignity-security foundation instead facilitates the recovery of a shared vision of the reality of the person that can root us back on solid ground (from which a stable and effective local and global health ecosystem can sprout).
- v. Underlying health ecosystem's AI digital transformation and technical reform is its ethical reform: healthcare is fundamentally the collective conviction of communal values, contextualized in society's political economics frameworks and operationalized technically in the provision of healthcare within the optimization of well-being. Could a more centralized or autocratic digital authoritarianism enable

more efficient societal well-being, but at the potential cost of repression, corruption, and long-term instability? Could a more democratic digital empowerment of healthcare enable a more sustainable and effective societal well-being, but at the cost of at least short-term polarization, inequities, and partisan infighting? Does the social algorithmization of the first regime as a means of political control (extending into healthcare) offer a greater risk to patient populations of the partisan demonization of the latter?

vi. AI health security, informed by this human dignity-security foundation, may thus be a noncolonial, substantive, and pluralistic framework for the effective global transformation of our shared health ecosystem that (in the words of the 1995 UN General Assembly address) avoids the "imposition of one social 'model' on the entire world," but rather empowers a "common effort to build the civilization of love," "founded on the universal values of peace, solidarity, justice, and liberty," animated by its "soul" which is "the culture of freedom" fulfilled in serving the common good safeguarding individuals' good (Paul, 1995). As AI opens a more expansive horizon of humanity and health's potential, so does it catalyze a more expansive metaphysical and moral rethinking globally as to whether we are satisfied with minimalist societal standards (i.e., health ecosystems avoiding lawsuits while maximizing profits nearly at all costs) or more expansive ones (encouraging our diverse cultures and political economic frameworks to consider that patients really do deserve a compassionate human presence caring for them as unique persons, rather than cold algorithmic "satisfaction" of needs for nameless consumers). This human dignity-security global approach underlying the international push for health AI security highlights the concrete present success and substantive potential of the below strategic, organizational, and technical AI healthcare advances.

(b) *Strategic: Strategic empathy*

- i. Modern healthcare cannot be delivered without global partners, supply chains, and enablers. Its AI-driven digital transformation only heightens the necessity of a globalized approach to collaborative competition in our pluralistic world, and the prerequisite "strategic empathy" to understand others' underlying constraints and drivers (including their individual agency and foundational ideologies), in contrast to "strategic narcissism" that only considers one's own constraints and drivers as relevant in our deeply interconnected and interdependent common home (Shore, 2014). It appears that strategic empathy may become increasingly instrumental in the AI-driven digitalization and competitive survival of healthcare systems, as it already is doing in the larger digital economy.
- ii. For instance, to better understand and work with China (and vice versa with the United States) if both persist in a rivalry-predominant

approach, the United States may benefit significantly from seeing China through Chinese eyes (and vice versa) as much as possible, as the pioneering Chinese military theorist, Sun Tzu, advised in the fifth century B.C., "If you know the enemy and know yourself, you need not fear the result of a 100 battles." Since its conceptual definition, strategic empathy has moved from political economics and international security to accelerating the competitive value differentiation of Big Tech in the digital economy, becoming central to the empathycentered enterprise-wide AI strategy of the \$2 trillion Microsoft (Denning, 2021). The 2010s sevenfold surge in market capitalization of the corporation correlated with the strategic pivot of its CEO, Satya Nadella, to begin with consumer needs and work backward to deliver customer-centric goods and services that optimize the user experience and thus overall value (transforming the organization through AI-accelerated Big Data-driven insights that enable rapid, adaptive value chains in a continuous iterative improvement cycle). Consumers get what they want (not simply desired products and services, but an integrated experience of one-stop shop convenience that increases consumer engagement longitudinally in a way that becomes a more longitudinal relationship, as consumers derive greater and long-term value, while producers generate greater and more reliable profit in this empathy-based business model). As more tech companies emulate elements of this empathy or consumercentric strategy (accelerated by AI), more tech companies as already discussed in the political economics chapter are exerting greater influence on healthcare systems as their ecosystem partners, while the abovementioned platform-enabled ecosystems are additionally grafting these drivers into emerging models of the future's health ecosystem, all in the latest evolutionary phase of healthcare as value based.

iii. Strategic empathy additionally reinforces the guard rails discussed in the political economics chapter, helping healthcare systems bridge competing US- and China-led global value blocks to deliver on their central mission of value-based healthcare. We had previously assessed how the early 20th century peak of European-led colonization gave way following WWI and WWII to the US-driven capitalist decolonization. democratization, globalization, digitalization of the later 20th century, before the height of the unipolar US-led liberal world order peaked in 2008 and began giving way to our current multipolar deglobalization world of the US-led democratic capitalist West, China-led more centralized or autocratic capitalist East, and more pragmatic Global South. As AI-enabled digital technologies become increasingly central to the digital transformation of healthcare, so too is the importance of strategic

empathy for health ecosystems to navigate the AI arms race of these global value blocks to cultivate (and sometimes even balance competing) ecosystem partners from different blocks (and the often competing and contradictory finance and regulatory frameworks for AI products and services, depending on their value block of origin). The West generally critiques China and Russia for their "digital authoritarianism" including in healthcare (using AI-enabled digital information technologies to repress domestic and foreign peoples through data centralization and informed state actions) and instead champions collaborative sovereignty (in which states can selfdetermine their own values and protect their citizens' privacy and agency free of undue coercion) (Makowska, 2022; Polyakova and Meserole, 2019). Such critics argue that autocratic regimes like in Xi's China will sacrifice individual rights and economic growth for maintaining political power, using even health like with China's zero-COVID policy through 2022 to exert greater societal control without commensurable health and health equity improvements, in addition to using biotech and health firms to obtain greater health and other sensitive personal information from nations globally for the Chinese Community Party to weaponize it for their political ends (Wertheim, 2021). The counterresponse particularly from China is that its centralized healthcare system, like its centralized political system, is more efficient, equitable, and stable than the polarized United States and the West, and that such efforts like its BGI Group (the world's largest biotech firm) attempting to obtain clinical and genetic data from foreigners including Americans are meant to help the rest of the world benefit from its superior stability and technological prowess, as its purported goal with its stability-focused foreign policy complementing its domestic policy of "common prosperity" (CSIS, 2022).

(c) Structural: Adaptive empowerment networks

i. Strategic empathy in a global dignity-security approach to the future's AI-enabled health ecosystems appears to increasingly rely on adaptive empowerment networks to leverage global resources and expertise for more efficient and equitable local healthcare. Yet a 2022 scoping review in Nature's Digital Medicine identified only 10 quantitative and/or qualitative studies on applied AI in low- and middle-income countries in the preceding 12 years (Ciecierski-Holmes et al., 2022). Only half specified the data sources and algorithms. And generally, all had limited success addressing largely prohibitive barriers of unreliability, costineffectiveness, limited user friendliness and data availability, lack of appropriate context-specific performance, and ineffective workflow enhancement. Though such problems are not specific to

- low- and middle-income countries, they are more pervasive, profound, and persistent than their rapidly digitalizing counterpart healthcare systems in high-income nations (generating not only the majority of AI technologies and successful use cases but also the research and practical guidance for such successes).
- ii. Microsoft and Novartis Foundation's 2020 report (with the African Union, WHO, and Facebook) still highlights the greater potential (and risk of being left behind) of low- and middle-income countries for AI-accelerated digitalization of their healthcare systems into the future's health ecosystems, as the COVID-19 pandemic era has already demonstrated how such nations have adapted such technologies (i.e., mobile phone trading platforms, e-commerce, e-banking, and blockchain) more comprehensively and rapidly than legacy systems in high-income countries (Broadband Commission, 2020). The report highlights the top AI health use cases accelerating global and public health performance in addition to healthcare systems includes PopHealth, clinical care pathways, patient-facing solutions, health operation optimization, and biomedical research. The six major areas to realize needs-driven mature AI in the health ecosystem include patients and health workforce, business model, design and processes, data and technology, ecosystem partnerships and stakeholders, and governance and regulation.
- iii. To accelerate this mature health AI particularly for low- and middleincome countries, there appears to be the growing need for such "adaptive empowerment networks" in which health ecosystem partners locally and globally leverage their capacities for sufficient individual and collective benefit to sustain substantive, efficient, and efficient partnerships that can adapt to ever-changing well-being needs, potential, technologies, and threats. Governments (fostering healthier, wealthier, and stable populations), healthcare and Pub-Health systems (delivering superior well-being outcomes at lower costs and disparities), technology and wider businesses (optimizing profit with sufficient transparency and benefit of ecosystem partners), and communities (receiving superior well-being, accessibility, affordability, and equity) can sustain such adaptive empowerment networks without sacrificing local governance, agency, and cultural nuances when the incentives and capacities are appropriately aligned.
- iv. The future's digital health ecosystem can thus benefit from network alignment in geopolitical, political economic, and ideological blocks forming value block suprasystems (i.e., West [i.e., EU, Commonwealth, AUKUS, NATO, the Quad, etc.], East [i.e., BRICS, SCO, GCC, etc.], and South [i.e., African Union, ECOWAS, etc.]) and institutional global suprasystems (i.e., UNESCO's Broadband Commission which drove the above report, WHO, public-private partnerships [i.e., UK's LifeBit and Hong Kong's Genome Institute], and

- professional and healthcare associations' affiliated universities and clinicians internationally).
- v. Key to healthcare's successful transformation into an AI-enabled health ecosystem is sustained growth, which is the product of increased number of workers and that of their productivity (workers using capital more efficiently) (Sharma, 2022). High-income countries need the labor force from immigration and value supply chains of low- and middle-income countries, and the latter need the former's market access, technology, and professional expertise. The mutual benefit of this relationship is further underlined by demographic decline (and in some areas even collapse) of the Global North (especially in China, Japan, South Korea, and non-French Europe). Adaptive empowerment networks for healthcare systems can build on this reality that drives much of modern value supply chains.
- vi. The "thickness" of such health adaptive empowerment networks may vary especially with political economic, cultural, and structural challenges. For example, the WHO may best prevent, predict, and mitigate pandemics with a global data architecture linking the world's national healthcare systems as a distributed cloud with edge computing and real-time access to and ambient always on analytics of health data required to rapidly identify and address new local infectious disease clusters before they become global. Nationalized and national public-private healthcare systems may optimize performance through a similar architecture in which telehealth extends the reach of hospitals, clinics, and well-being hubs. Though such collaborative and technical growth will likely be hampered by local concerns about data privacy and security, the trajectory toward greater rather than reduced data integration and more robust architectures regionally, nationally, and globally is expected to stably continue.
- vii. Cloud computing is expected to become increasingly effective and efficient as the density and comprehensiveness of such data architectures grow among adaptive empowerment networks, like Moderna (with its AI-driven continuous operational and technical improvement cycle) and the US emerging health business model of segmented integration of care (as diverse segments or ecosystem partners compete for market share of digital capacities regionally and globally delivering greater value in the networks for the ultimate collective benefit of the network and the other partners). Consider the strategic partnerships led by number and size of US acquisitions of health providers by payors and businesses. November 2022 marked the impending \$9 billion acquisition of Summit Health (network of 370+ medical practices and urgent care centers) by the commercial pharmacy chain, Walgreens, with a minority owner in the venture

being the large health insurer, Cigna (Cooper, 2022). The deal notably includes a part-owner in Summit Health, Warburg Pincus private equity firm, which spans health IT and hospital revenue cycle management in its portfolio. Such adaptive empowerment networks are expected to grow in the number, capacity, and complexity of such ecosystem partners as well as geographic regions (including low- and middle-income countries) to leverage the synergistic strengths of the health ecosystem partners benefiting from the needed growth. Such efforts are in parallel with more local PubHealth efforts including "Dads on Duty," a program began by fathers of low-income high school students in which those vetted by a security firm are invited to be a mentor presence at an innercity minority predominant school, which has since noted a significant reduction in teenager and gang violence with reduced police presence, as the students increasingly embrace the more welcoming supportive presence of the dads (Wyatt, 2022). The similar grassroots initiative, the Friendship Bench, began in Zimbabwe with psychiatrists training and then deploying over 400 grandmothers for free evidence-based talk therapy for over 30,000 people (in a nation of 16 million with only 12 psychiatrists) (Nuwer, 2020). A 2016 Journal of the American Medical Association randomized controlled trial confirmed the program's clinical success improving depression, similar to results from subsequent program monitoring in its scale up to other nations including the United States (Chibanda et al., 2016). Such local efforts when paired in AIenhanced adaptive empowerment networks may allow effective testing and scale up of local programs throughout the networks.

- viii. In the more clinically focused context, AI-enabled tele-ICU has already been demonstrated to rapidly and adaptively scale up limited ICU resource and workforce capacities, as in the case of two Israeli hospitals using AI-driven predictive analytics paired with remote field ICUs for COVID-19 patients to project who will likely worsen clinically and how to intervene successfully before they do (all the while leveraging the expertise of a central remote command center with greater community reach) (Lovell, 2020). Such adaptive empowerment networks have subsequently been scaled internationally with proof of concept in technical and clinical deployment.
- (d) Local: Adaptive embedded clinical trials and digital twins
 - i. A particular type of adaptive empowerment networks are adaptive embedded clinical trials, which seek to more rapidly, efficiently, and fairly translate appropriately designed clinical trial evidence into life-saving evidence-based standards of care by embedded trials in at-scale healthcare delivery (Anastasijevic, 2021). Of the 2610 clinical trials of repurposed drugs performed in the first year of the COVID-19 pandemic, only 5% were appropriately designed and

enrolled. Additionally, the vast majority not only of patients with COVID-19 but all health conditions receive care in distributed rather than centralized academic medical centers, and they do not enroll in the clinical trials, which predominantly are conducted in such academic centers (despite the reality that the bulk of cutting-edge medical innovations are introduced in those trials at those centers). Therefore, Mayo in 2021 partnered with the US FDA, Harvard University, and Duke University among others to launch a national coalition to reverse such trends by bringing the expertise and clinical trials of major academic medical centers to community healthcare systems (particularly in underserved communities), accelerated by AI-augmented digital technologies, to enable at-scale clinical trials embedded in routine healthcare system operations nationally (so patients who may benefit from more advanced therapeutics can have expanded opportunities to receive care through such trials that are correctly designed, efficiently enrolled, and completed and translated into timely clinical decisions).

ii. In parallel with such trials embedded as part of and as an adjunct to routine clinical care, "synthetic data" are increasingly being manufactured, modeled, and deployed by pharmaceutical and medical device companies with research-orientated healthcare systems to accelerate the translation of research findings into enhanced clinical care (Hersey, 2022). "Digital twins" is a particular type of such data in which virtual human subjects are created in trials' control arms to reduce the number and potential harm of real human subjects in such trials, and thus accelerate sufficient enrollment, analysis, and clinical translation of such trials (without sacrificing sufficient external and internal validity of trial design). Nature and BMJ reviews demonstrated respectively that hundreds of deep learning (DL) models predicting COVID-19 diagnosis and prognosis based on medical images in addition to machine learning (ML) models adding clinical data largely failed to be of sufficient validity and clinical utility to justify safe and effective use in actual healthcare delivery. To improve their success (while reducing the often prohibitive time navigating stringent data privacy rules), large and rapid amounts of data can be generated through such digital twins to speed effective clinical trials to successful clinical translation, without cutting methodological corners which would jeopardize the reliability and safety of such research findings for real-time clinical care. Washington University in St. Louis for instance built the National COVID Cohort Collaborative after 2019, spanning 72 institutions and 13 million patients, and has not only become one the largest deidentified COVID-19 datasets to date but also allowed demonstration that its derivative synthetic data accurately represent the real patients (from which the data are derived) and are even more secure (making it more difficult to

reidentify subjects compared to conventional nonsynthetic data methods). The private firm, Unlearn.AI, has further demonstrated that digital twins not only allows faster trial enrollment but also that it can more comprehensively inform how a real subject would have responded to different treatments in addition to obtaining European Medicine Agency and US FDA drug approval based on such synthetic data.

iii. Of the 772 research articles on AI in clinical trial development up to 2022 assessed in a scoping review, only 5 included quantitative assessment of AI efficacy, though all the studies demonstrated promising results particularly with AI increasing recruitment and completion speed with comparable performance relative to traditional non-AI methods (further supporting the promise but still room for growth in AI-enabled trials, especially with embedded design and digital twin augmentation) (Cascini et al., 2022).

(e) Operational: Quantum health

i. Global consensus increasingly supports the unprecedented potential of quantum computing to further speed the AI-driven digitalization of our world and particularly healthcare (IBM, 2022). Utilizing quantum mechanics (a probabilistic-informed mathematics modeling of the motion and behavior of subatomic particles), quantum computing is progressively leapfrogging classical computing at more rapidly, efficiently, and successfully solving complex problems by creating multidimensional spaces that model the patterns joining individual data points. The hospital-business partnership of Cleveland Clinic and IBM in their Discovery Accelerator produced the first healthcare quantum computer with a launch point of early 2023 for the private sector onsite, "IBM Quantum System" (Reale-Cooney and Benchaita, 2022). Though the technology is still relatively young, its practical application and institutionalization in healthcare is already steadily growing through such adaptive empowerment networks, enhancing the partnership's existing portfolio accelerating translational clinical research with AI-based hypothesis generation, cloud-based end-toend chemical compound discovery and robotic lab control, and insight generation from unstructured technical literature.

(f) Functional: Liquid AI's cloud-based predictive EHR

- i. Liquid AI: AI-enabled health ecosystems likely will require increasingly more powerful, real-time, ambient, and self-adaptive AI that more and more approximates artificial general intelligence (AGI) that truly "thinks" for and by itself with minimal human input. A potential technical breakthrough toward this is liquid AI, particularly with significant advances from MIT with 2021 adaptive algorithms and 2022 differential equations (Ackerman, 2021; Tarantola, 2022).
- ii. MIT developed "liquid" neural networks that adapt their foundational mathematical equations in response to changing real-time (time

sequence) data inputs to optimize ultimate model performance, with broad applications for medical diagnostics and imaging, autonomous driving, robotics, and NLP. The dominant contemporary artificial neural networks (ANNs) included in healthcare narrowly focus on specific tasks (as the algorithms' equations are fixed at the training phase and so often struggle to adapt to real-world data, applications, and time-sensitive unpredictable changes after it). In contrast, MIT's liquid ANNs are by design empowered to change their parameters according to the underlying nested differential equations that "flow" with the new, often noisy, messy, fast-moving, unpredictable data (like unexpected surges in trauma patients or rapid emergence of high-virulent pandemic viruses). Liquid AI's adaptability additionally enables superior explainability (i.e., by better unpacking the "black box" algorithms by seeing how model outcomes change as neural representations are changed), accuracy (better than competing stateof-the-art time series models), and reliability with preserved efficiency (with smaller but richer nodes) compared to legacy ANN.

- iii. Additionally, MIT's 2022 "closed-form continuous-time" (CfC) ML advancement appears to have resolved the century-old mathematical problem that previously has made scaling of ANN's prohibitively computational expense. By replacing the differential equation defining neuron computation (defining the interaction of two neurons through a synapse) with a closed form approximation, the speed and efficiency of liquid ANNs could be preserved without the costly numerical integration. This allows CfCs to be "causal, compact, explainable, and efficient to train and predict" and so enable "trustworthy machine learning for safe-critical applications" including real-time enterprise-wide AI strategy and clinical decision-making augmentation. A differential equation is a formula modeling a system at discrete steps in a process, but this becomes computationally prohibitive when you have to scale this modeling at every node (or step or point), like modeling the 86 billion neurons in a single human brain or the trillions and trillions of elements critical to a health ecosystem functioning. Instead, CfCs allow the entire system to be modeled in a single computational step with fewer, faster, and more expressive neurons. Mathematically, CfCs make plausible eventual "out-of-distribution generalization" in such contexts as teaching an ML model how to detect different cancers on a radiographic image (i.e., after training and validating the model on many CT scans) but unleashing its ability to learn, adapt, and improve itself in different environments with different often noisy inputs (from different patients, cancers, clarity of images, etc.).
- iv. AI-enabled EHRs may be one of the highest value-added use cases in the near to intermediate term for workflow bottlenecks and targets for

clinical efficiency gains with liquid AI. Amid declining and in some areas collapsing fertility rates in the Global North and worsening global shortages of physicians, there are unsurprisingly surging labor costs (remaining the top expense for hospitals at over 50%) and declining operating margins (falling even in negative range with the COVID-19 pandemic even in the United States) (AHA, 2022). Concurrently, there are growing all-time record required times for clinician documentation (with US physicians pushed to spend four times longer than non-US physicians on EHR note writing to comply with increased regulatory and billing burdens for notes [often in the name of improved healthcare value and efficiency], leaving US primary care physicians in particular to spend the majority of their work days writing notes rather than seeing patients) contributing to the up to \$1.7 billion annual costs of physician burnout, and thus furthering clinician shortages (Finnegan, 2018). To address these clinical inefficiencies and workforce threats while improving diagnostic and treatment effectiveness (and thus patient safety), there is a growing push for AI-enabled EHRs. For instance, a 2022 Nature study demonstrated that "PhenoPad" note-taking interface with EHRs improved efficiency and clinical completeness through AI (with natural language processing [NLP], automatic speech recognition, and clinical decision support for PCPs), while AI-enabled "ambient clinical intelligence" with "computer-assisted physician documentation" consistently has been shown to expedite capture of necessary patient information elements within existing clinician workflows (Davenport et al., 2018; Nuance, 2022).

v. The most substantive and institutionalized advancement in AIenabled EHRs may be coming from Google's healthcare partnerships as (notwithstanding the risks of digital colonization noted in the political economics chapter) its Google's 2017 patent appears to be progressing toward deploying its own DL-empowered EHR with integrated cloud computing and outcome prediction, in parallel with its 2022 agreement with the largest EHR vendor (Epic) to migrate the EHR to Google Cloud, beginning with the US-based Hackensack Meridian Health System of 17 hospitals in November 2022 (Landi, 2022). This adaptive empowerment network pairs Epic's existing clinical workflows (with its deep embedded health data architecture, functionality, and clinician familiarity) with Google's ambient intelligence (detecting patterns for clinical and operational decision support) and healthcare data engine accelerators (with personalized data infrastructure configurations, Looker dashboard templates, and Big-Query data models). Together, this enables partnering healthcare systems to leverage Google's industry leading data infrastructure to empower enhanced data security, interoperability, liquid accessibility,

- privacy controls, and compliance by design (including Health Insurance Portability and Accountability Act [HIPAA], related regulations, and required billing).
- vi. Pairing liquid AI with the growing technical advances and strategic institutional scale-up of AI-enabled EHRs strongly suggest a realistic and effective partnership to better realize the already present successes—but more in real time, scale, and comprehensive functionality.

9.5 The future's (AI) health ecosystem DNA: $H = AE^2$

In this final section of the book, we are finally in a position to integrate the preceding concepts and cases into a single unified vision as a simplified and synthetized formula that may help humanity unlock the future of (optimized and humane) healthcare, by beginning to grasp what may be its essential system DNA (drawn as a convergent consensus from different sciences, states, systems, and cultures). We began this book to understand how and why AIdriven digitalization is rapidly transforming modern healthcare into the model of what a growing shared vision suggests is becoming the future's health ecosystem, housed in our ideologically divided but practically globalized world. We sought to understand healthcare, where it came from, what it is working to address now, and where it may (and should) be going. Thus, we had to talk about how AI is rapidly touching and transforming all of healthcare, from its trajectory to its framework to even its foundation. And we also had to consider human equity, the counterbalance to the unprecedented efficiency gains AI is already empowering healthcare systems to achieve. AI is a powerful tool, but we need a unifying vision informing how we use it based on what kind of healthcare system we want to build for ourselves and our children, based foundationally on what we believe is good healthcare and ultimately what we believe is good and what is good for human persons.

Toward that, we have progressively built up to the definition of the future's health ecosystem in which data and well-being are integrated and driven by AI, leveraging diverse partners globally to optimize local governance that ultimately facilitates well-being equitably. But as a practicing physician in modern medicine, I cannot treat a patient correctly unless I have diagnosed the person correctly. The discrete definition of the problem informs the discrete solution for it. Though such growing consensus on high-level descriptions of the future's health ecosystem (i.e., from Deloitte, McKinsey, or NEJM) may be helpful and eventually even accurate, it may be prohibitively imprecise as an amorphous conceptual blob to be actionable now (as a defined problem-solution relationship) in terms of progress toward a concrete and desirable state. So we have been working this whole book increasingly to the definition and defense of the future's proposed "thinking healthcare system." "Thinking" invokes the

simplifying integrated complexity of our brains, harnessing billions of diverse components (i.e., synapses, neurotransmitters, etc.) and processes (i.e., biochemical, electrical, etc.) that are orchestrated with an elegant unity of ultimate purpose—coordinating the diverse organs of our bodies for individual through communal survival. Similarly, the clinical analogical version of our formulaic definition of AI health (as a thinking health system) sought to detail the individual content and relationship among the health ecosystem's various components (as organ systems)—PubHealth (skeletal), PrMed (muscle), patient safety (immune), politics (respiration) with economics (GI), ethics (endocrine)—and processes including HealthBD (cardiovascular), all raised to the exponential power of AI (nervous). AI can and is rapidly increasing its track record integrating, digitalizing, and electrifying these modern components and processes of our fragmented and largely analog modern healthcare systems to empower them with a unifying intelligence and (if we design and optimize it for such) orientation toward a shared desired end, the common good (especially in its particularly dimension of equitable well-being).

We have thus sought to put "meat on the bones" of this formulaic vision throughout the book to make the AI digital transformation of modern systems a more concrete, intelligible, accessible, and actionable vision for you, the reader, and the rest of the broad audience of diverse stakeholders required to achieve this great shared leap forward. But specifically, our mathematical version of the AI Health formula sought to practically guide how this process can be realized by understanding the above system components, processes, and relationships in reference to the system's operationalization of them:

$$AI\ Health_{Mathematical} = \left(\text{HealthBD} \times \left[\overline{Delivery} + \sum_{n=1}^{\infty} \{ \text{PrMed cos } Delivery + \right. \right. \\ \left. \text{PubHealth sin } Delivery \} \right] \right)^{AI-VBHC}$$

The dynamic balancing act of the patient and the population, operationalized in the dynamic balancing act of PrMed and PubHealth (whose joint function can facilitate well-being) can be optimized by empowering it with HealthBD (or smart data). But to unite these two, their integration through AI-VBHC (or AI-enabled value-based healthcare) can put the complementary relationship of efficiency and equity at work for every patient and thus every population (by putting efficiency and equity at work for each other). Rather than prioritizing one or the other, we have explored how both can be practically maximized in a way that produces their net vector of a third or middle way between both of them, toward the reality of the person which informs the common good of the global human family (which the UN's UDHR at the advent of modern globalized healthcare articulated, since becoming the charter of our modern world echoed or ratified by the vast majority of our constitutions, conventions, and communities). We have explored this operationalization of this efficiency-equity or value-virtue relationship as it is strategically, operationally, and even mathematically translated into healthcare system form and functioning, including with real-time concrete application for such a clinically complex challenge as cardiac arrests (Monlezun et al., 2022). We have considered how optimized healthcare efficiency may increasingly require embedded AI that has organizational and technical end-to-end integration (in its business model and intelligence-driven workflows both at the management and clinical levels), grounded in a moral integration of the diverse belief systems and cultures in which the healthcare system is contextualized, collectively producing a "resilient integration" that defines the boundaries of the system, and thus how its components and processes function within them. Curiously, it may actually be equity that finally unlocks the next frontier in this AI-enabled healthcare, as growing performance improvements for a progressively small percentage of the population can produce excessively destabilizing effects on the entire healthcare enterprise (and so jeopardize the performance for this elite subpopulation not just the entire population). And we explored how this societal equity is further supported by the personal dignity, community diversity, and societal security by a broad consensus of the world's pluralistic belief systems (as articulated by PSC). We then delved into concrete use cases of AI-empowered healthcare that can be efficient and still equitable in the above different components of system functions, including how they can be integrated seamlessly including the AI-driven computational ethical and policy analysis or AiCE.

This brings us to the organic formula or system DNA of the future's thinking healthcare system to unify these concepts and cases, illustrating how data (with AI-enabled infrastructure) and well-being (with AI-enabled organizational infrastructure) can be integrated via the function of resilience integration in the form rooted in the system's foundational moral interoperability:

$$H = AE^2$$

This final simplified formulaic definition of the proposed essence of the thinking healthcare system represents Health (H) as the product of AI (A) and equity (E) squared. This formula is structurally similar to Einstein's famous $E = MC^2$ (in which E or energy is understood as the product of mass or m and c or the constant for the speed of light squared), in which energy and mass are essentially interchangeable (under the right conditions), or unique manifestation of the same reality. Similarly, this system DNA formula proposes that "human health" and "artificial intelligence" can be interchangeable. Though controversial just as a statement, the book has gradually sought to demonstrate how it can be substantively and empirically clear already in current practice. We have detailed how modern healthcare systems, though with brilliant capacities and breakthroughs, still consistently do not reliably deliver affordable,

accessible, quality care that optimizes well-being, either for persons or populations. But we have also seen how AI in a growing number of cases can consistently deliver desired outcomes in multiple technical and economic sector contexts, including and progressively with healthcare by doing it efficiently (with increasing effectiveness at scale with decreasing costs). Yet without equity, AI efficiency is ultimately undermined and compromised, but AI-HealthBD driving efficiency at scale can approach the approximation of equity (by effectively delivering value-based care fairly at the population level). Efficient AI healthcare at scale signals that individual performance of well-being optimization has been so achieved as it can be expanded to the communal and even global level, representing therefore mature AI-empowered healthcare that essentially is equity exponentiated (producing orders of magnitude in health improvements with each additional unit of AI-driven equity growth). Thus, the future of health optimized may rapidly become AI that is optimized (both scientifically and ethically). The energy powering the future of humanity is the health of humanity which can sustain us, through the critical mass of our best scientific and ethical creativity of AI worthy of the persons it is meant to serve in the thinking healthcare system (consistently mindful of this primary mission to advance the common good of the global human family).

This common good or human reality can thus sustain the needed foundational moral interoperability uniting the values and value of our future's thinking healthcare system, consisting of the dignity-security interface as the backbone foundation of our planet's diverse peoples and local healthcare systems, like the deoxyribose (sugar)-phosphate strands of DNA's double helix encoding and enabling our unique human lives. It can ground and orchestrate the dynamic balancing act or creative tension of the complementary base pairs of efficiency-equity, data-well-being, science-ethics, and the remaining components of the system discussed in the above figure. This simplified and synthesized formulaic definition of the future's healthcare system may thus allow us to choose a third way or a better way, instead of having to choose between efficiency in one direction or equity in the other, data or well-being, dignity or security, East or West, and North or South. Rather than being left or right, this third direction may be one forward, one that is a future for humanity and healthcare that we can commonly desire, hope, and work toward on unique paths toward a common goal (potentially aided by this actionable formulaic vision illustrating remaining problems and even the early forms of their AI-enabled solutions). This is not a full-proof roadmap but rather a practical realization that a thinking healthcare system with intelligent strategies and structures fixed on the common good can respond with increasing effectiveness, efficiency, and equity to the unending challenges that threaten systems' survival (by responding successfully to the unending challenges that threaten the survival of the populations they serve). In such a formulaic DNA of the future's thinking healthcare system, may it

entail the very seeds of its survival, enabling it to grow, adapt, learn, and think (and so ultimately care), as is required by the dignity and security of the humanity for which it is ultimately created. Its final exact form is unknown, but its function is not (nor the likely contours, components, processes, and relationships which frame what is possible and needed, which in turn practically catalyzes and informs the evolution of the thinking healthcare system). So can this organic DNA of a formula defining the future's thinking healthcare system be already now actionable, and eventually worthy, of our patients now and those our children will become? Can this system DNA simultaneously be a blueprint and a roadmap, both a bold vision and a practical plan? By becoming more intelligent, and thinking more deliberately about who we serve and thus how we design and optimize our modern healthcare systems with efficient and equitable AI, can our healthcare systems become more compassionate, more human, more of the future we deserve now? We began this book with a hurricane and a hospital, and we end with the health and hope for humanity that is as possible as it is needed—with your help.

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The Thinking Healthcare System

Artificial Intelligence and Human Equity

Dominique J. Monlezun, MD, PhD, PhD, MPH UT MD Anderson Cancer Center, Houston, TX, United States

The Thinking Healthcare System: Artificial Intelligence and Human Equity is the first comprehensive book detailing the historical, global, and technical trends shaping the evolution of the modern healthcare system into its final form—an Al-driven thinking healthcare system, structured and functioning as a global digital health ecosystem. Written by the world's first triple doctorate trained physician-data scientist and ethicist, and author of three Al textbooks and over 350 scientific and ethics papers, this indispensable resource makes sense of how technology, economics, and ethics are already producing the future's health system—and how to ensure it works for every patient, community, and culture in our globalized, digitalized, and divided world.

Providing clear descriptions and concrete examples, this book brings together Al-accelerated digital health ecosystems, data architecture, cloud and edge computing, precision medicine, public health, telemedicine, patient safety, health political economics, multicultural global ethics, blockchain, and quantum health computing, among other topics. Healthcare and business executives, clinicians, researchers, government leaders, policymakers, and students in the fields of healthcare management, data science, medicine, public health, informatics, health and public policy, political economics, and bioethics will find this book to be a groundbreaking resource on how to create, nourish, and lead Aldriven health systems for the future that can think, adapt, and so care in a manner worthy of the world's patients.

Key Features:

- Details the first comprehensive, global, and multidisciplinary analysis of the Al-driven transformation of modern healthcare systems into their definitive digitalized form that will dominate the future
- Provides clear descriptions and concrete examples of Al-informed value-based healthcare, digital health ecosystems, data architecture, cloud and edge computing, precision medicine, public health, telemedicine, patient safety, health political economics, multicultural and embedded global ethics, blockchain, Al security, health security, digital twins, and quantum health computing
- Serves as a practical blueprint, roadmap, and system DNA for creating the future's healthcare system that integrates
 efficiency and equity to accelerate the treatment (and in some cases even cures) for some of our world's most
 urgent, immediate, and impending global health challenges and crises

About the Author:

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